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XEROX INTERNAL REPORT

RETROSPECTIVE COHORT STUDY OF MORTALITY OF XEROX EMPLOYEES

(Vital status tracked through December 31, 2006)

A Standardized Mortality Ratio Analysis under the Direction of Xerox Corporation, Environment, Health and Safety Staff and Consultants

SANITIZED VERSION

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Written By: ________ Date: 5/20/11
Susan B. Rawleigh, MPH, MS

Reviewed By: ________ Date: June 2, 2011
Jonathan M. Samet, MD, MS

Authorized By: ________ Date: 5/20/11
Larry R. Glass, Ph. D., MPH

STUDY PERSONNEL

XEROX PERSONNEL

Larry R. Glass, Ph.D, MPH
Principal Investigator
Manager of Environmental Health & Toxicology
Environment Health & Safety
Xerox Corporation

Susan B. Rawleigh, MPH, MS
Study Coordinator
Epidemiologist, Environment Health & Safety
Xerox Corporation

Norma I. Horn
Health Research Assistant, Environment Health & Safety
Xerox Corporation

CONSULTANTS

Jonathan M. Samet, M.D., M.S.
Professor and Chair, Department of Preventive Medicine Director,
USC Institute for Global Health Keck School of Medicine
University of Southern California/Norris Comprehensive Cancer Center

Michael E. Tomb
President, Informatica ECS, Inc.
Rochester, NY 14604

Stephen J. Gange, Ph.D.
Professor and Deputy Chair, Department of Epidemiology
Johns Hopkins Bloomberg School of Public Health

Alison Abraham, PhD, MS, MHS
Johns Hopkins Bloomberg School of Public Health

Gayle Springer, MLA
Johns Hopkins Bloomberg School of Public Health

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EXECUTIVE SUMMARY

This report describes the findings of an epidemiological analysis of mortality among Xerox employees. The overall goal of the study was to assess if occupational exposure to toner, either during the manufacturing of the toner itself, or during the servicing of copying equipment, had any adverse effects on employee mortality. The study was carried out as part of a longstanding and ongoing effort by Xerox to monitor the health of its employees and to understand the biological effects of toner. Toner is made up of particulate material containing particles of a size that can be inhaled into the lung. Because recent studies in the scientific literature have shown an increase in the risk of premature mortality and cancer associated with long-term exposure to particulate matter air pollution in the general population, Xerox has also sought to ensure that similar effects were not being experienced by its toner-exposed workers. Additionally, there has been long-standing interest in the effects of occupational exposure to carbon black, a key component of toner.

The study design used is called a "retrospective cohort study". In this design, the workers are tracked over time to capture any deaths and their causes; it is termed "retrospective" because all events are in the past, and the data are gathered using a variety of record systems that have collected and retained the needed information. To determine if toner exposure does increase the risk for mortality for specific causes of death, comparison was made between the mortality rates in the toner-exposed workers and non-exposed workers to the US population in general. A ratio of the age-adjusted rates, called the standardized mortality ratio, or SMR, was used for this comparison.

The study group, called the cohort, was assembled from work records and included 33,671 workers, employed between 1960 and 1982, that met the eligibility criteria for the study. For all work experience at Xerox through 2006, they were classified as exposed or not exposed to toner, based on their work histories; once workers were classified as exposed, they remained in this category, even if they returned to a job not involving toner exposure. The vital status (i.e., dead or alive designation) of each worker was determined through the use of various national databases. Information on the cause of death was obtained and coded using a widely utilized and standard classification scheme. Vital status was tracked through the end of 2006.

In general, there was a pattern of lower mortality in the overall Xerox population than expected compared to US mortality rates. The SMRs for all-cause mortality were 0.75 and 0.5 for white and non-white males, respectively; and 0.88 and 0.72 for white and non-white females, respectively. This is consistent with the "healthy worker effect", typically seen in occupational cohorts whereby workers have lower death rates than the general population because workers are generally healthier than those who are not working. In addition, the SMR estimates for all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes, conditions for which an increase in mortality due to exposure to particles could be hypothesized, were all lower than 1.0 in toner-exposed males (white and non-white) suggesting that toner exposure in an occupational setting does not cause an increase in mortality for any of these conditions. Similarly, no significant increases were seen in females for all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes.

Occupational mortality studies like this study typically have some well characterized limitations that may influence the results. Information on disease risk factors for individuals may be lacking. For example, this study, like most occupational cohort studies, lacks data on smoking so that it is difficult to explain an excess of lung cancer in the white female control population. However, this increase was observed in the non-exposed population so the increase is not related to exposure to toner.

Similarly, the study also lacked data on risk factors for breast cancer (e.g., having no children or having a first child at an older age). Increased risks of breast cancer have been reported in the literature in a number of occupational groups and are often attributed to patterns of parity and maternal age at first birth. The increase observed in breast cancer in the white female population of Customer Service Engineers (CSE) in this study was not observed in the toner-exposed manufacturing group and therefore might be due to differences in the distribution of risk factors; however, the requisite data are not available to substantiate this hypothesis.

Increases in digestive cancers in the white male control population (from Webster, NY) that were observed in this current analysis as well as the previous analyses of this cohort are probably in part a consequence of the selected reference population (e.g., general US population) used in this study. When NYS rates were used as the reference rates, the increases were no longer statistically significant.

In spite of these limitations, the study provides useful information on patterns of death among Xerox workers, particularly those who have been occupationally exposed to toner. The results of this analysis are consistent with the general mortality patterns among healthy working populations. There was no evidence that occupational exposure to toner increased the risk of all-cause or cause-specific mortality. However, ongoing follow-up of the cohort will provide useful information, with a repeated assessment of mortality patterns as this population continues to age. Such tracking is needed to assess potential long-term consequences of toner exposure as the cohort continues to age.

INTRODUCTION

Adverse health effects due to acute and chronic inhalation of fine particles have been an area of interest and a growing concern in the current scientific literature for the past several decades. The general population is continually exposed to airborne particles, from natural and man-made sources that are ubiquitous indoors and outdoors. An association between mortality and chronic exposure to ambient particulate pollution has been found in a number of studies [1, 2, 3] and this finding has been part of the rationale for a strengthening of standards for airborne particulate matter in the United States and elsewhere. Studies in the general population also link particulate matter to a wide variety of health conditions and diseases, such as respiratory and cardiovascular disease [4, 5] and diabetes [6].

Certain occupational groups have even higher exposures to particulate matter than the general public, and the adverse health effects due to inhalation of some particulate agents are well documented, such as the pneumoconiosis and the lung cancer risk associated with asbestos. Given findings of these increased health risks associated with outdoor air pollution and with specific occupational agents as noted above, exposure to airborne particles in the workplace is a potential concern. Xerox Corporation, as part of its longstanding and ongoing commitment to workplace health and safety, has conducted two multi-decade studies of its workers with occupational exposures to toners.

Toner

Toners are fine powders composed of plastics, colorants and minor quantities of functional additives (e.g., silicon dioxide, titanium dioxide). Toner formulations vary from machine to machine and from manufacturer to manufacturer. Depending upon the specific machine application, either styrene-acrylic, styrene-butadiene or polyester polymers are the major component of toner. Carbon black or iron oxide are used as colorants for black toners, while various dyes or pigments are used for color toner. The majority of carbon blacks currently manufactured have small quantities of organic compounds, including polycyclic aromatic hydrocarbons (PAH) and nitropyrenes, adsorbed onto their surface [7]. The levels of these contaminants in carbon black vary with the manufacturing process used [8]. Ames mutagenicity assays in the 1980's raised concerns about a mutagenic response resulting from these contaminants. In 1980, Xerox introduced a standard to control the level of PAHs (PAH levels – total specified < 1ppm; non-specified < 10 ppm) and nitropyrenes (< 1.2 ppm) in the carbon black that they used. In 1990, Xerox further reduced the level for nitropyrenes to < 0.15 ppm. Levels of such contaminants have since become negligible in Xerox toners[9].

Under normal operating conditions, toners are entirely stable and no significant amount of decomposition takes place. They merely flow and adhere to the paper upon the application of heat, or heat and pressure, depending upon the specific machine. Generally, the toner is supplied in the form of a developer mixture consisting of a carrier material and toner. Carrier beads (non-respirable; > 30 µm) primarily serve to facilitate the transfer of toner beads from the feeding system to the paper. Xerox carriers are based on special grades of sand, glass, steel or ferrite materials. They are generally coated with a small amount of special polymer to achieve the desired functional behavior in the xerographic equipment [10].

Historically, the median particle size of toner ranged from 8 to 10 micrometers and toner was made by a stepwise mechanical process involving melt mixing of the raw materials; grinding and screening to produce a fine powder; followed by the addition of surface additives and a final screening. In 2002, advances in technology led to a new chemical process used to grow toner that resulted in smaller and more uniform particle sizes. This study deals primarily with exposures from conventional toners.

Carbon Black and Titanium Dioxide

Two of the ingredients in toner, carbon black and titanium dioxide, have been classified by the International Agency for Research on Cancer (IARC) as "possibly carcinogenic to humans" (Group 2B). Carbon black is used as the colorant in black toners and employees are exposed to it as a raw material in toner manufacturing and bound within the toner particle in black toner. The most recent IARC review in 2006, found that there was sufficient evidence in experimental animals, but inadequate evidence for the carcinogenicity of carbon black to humans. However, IARC noted in its evaluation that "No significant exposure to carbon black is thought to occur during the use of products in which carbon black is bound to other materials, such as rubber, printing ink, or paint" [11]. A study by Fong et al., using scanning electron microscopy (SEM), transmission electron microscopy (TEM) and laser diffraction particle size analyzers showed that carbon black was bound within the polymer matrix of the toners tested and they were unable to detect any free unbound carbon black in the toners examined. Thus, evidence indicates that carbon black in commercially available toners is bound within the toner particle and that no significant exposure to carbon black occurs during the use of toner as the end product [12].

Titanium dioxide is also found in toner in small amounts (< 5 %) as a functional additive on the surface. Titanium dioxide was originally classified by IARC in 1989 as "not classifiable as to its carcinogenicity to humans" (group 3) but that classification was recently changed to "possibly carcinogenic to humans" (Group 2B) in 2006 due to sufficient evidence in experimental animals, but inadequate evidence that titanium dioxide is carcinogenic in humans [11].

Literature Review of Toner

Toner itself has been studied in animals and to a lesser degree in humans. Acute toxicity studies on Xerox toners, including acute oral toxicity in rats, acute dermal toxicity in rabbits, acute inhalation toxicity in rats, eye irritation in rabbits, skin irritation in rabbits, and skin sensitization in guinea pigs consistently showed that all toners tested were practically non-toxic and that they were nonirritating to the eye and nonirritating/nonsensitizing to the skin[13]. Animal models have also been used to explore the potential carcinogenicity of inhaled toner. Inhalation studies in rats and hamsters provide no indication of an increased risk of lung tumors in rats exposed to high levels of toner, though there was evidence of particulate matter retention, inflammatory response and pulmonary fibrosis[14,15,16,17,18,19,20]. In a 2-year study, conducted by Xerox Corporation in rats, lung changes seen at high doses (16 $^{mg}/_{kg}$) and to a lesser extent at the moderate doses (4 $^{mg}/_{kg}$) were identical to the characteristic signs of lung overloading which is a series of generic responses to the presence of large quantities of benign dusts retained for extended time periods in the lung. No changes were seen at the low dose (1 $^{mg}/_{kg}$) which is the most relevant level with respect to potential human exposures [21,22,23]. This study used a specially prepared "test toner" that was enriched about ten-fold in respirable size particles relative to commercial toner such that it was about 35 % respirable according to ACGIH criteria[22].

In 1980, Ames assays done with extracts of xerographic copies and toner raised concerns about mutagenic responses resulting from a contaminant (nitropyrene) created during manufacture of some carbon blacks used in black toner [24, 25]. Additional in vitro testing done on Xerox toner 1075 in 1999, after Xerox had introduced standards to control levels of PAH and nitropyrenes in the carbon black used, found toner to be non-mutagenic in a battery of short-term assays (Ames Salmonella/microsome assay, mouse lymphoma assay, in vitro sister chromatid exchange assay in Chinese hamster ovarian cells and in vitro BALB/3T3 cell transformation assay) [26]. An *in vitro* study of the effect of toner on alveolar macrophages indicated that toner dust was toxicologically inert in this assay [27]. Another recent study evaluated the genotoxic potential of 3 non-Xerox black toners in the comet assay, the cytotoxic block micronucleus test and the erythrosine B assay. The toners were found to not reduce cell viability but they did induce DNA damage and formation of micronuclei. The authors suggested that metals and metalloids (components of magnetite) or PAHs (component of carbon black) were responsible for the genotoxic effects. The levels of PAH in these 3 toners (Kyocera TK-16H, Kyocera TK-17 and Hewlett-Packard LaserJet C4092A) were reported to be 539, 2623 and 405 $^{\mu g}/_{kg}$, respectively [28].

In a study that used intra-tracheal instillation of toner (every other day for four times) in mice, exposure to toner at 40 $^{mg}/_{kg}$ inhibited the normal growth of mice and induced significant inflammatory responses and lesions in lung tissues[29]. In another carcinogenicity study, known as the"19 dust study", two groups of rats were given intratracheal doses (once weekly for either 10 or 20 times) of the Xerox "test toner" used in the inhalation study carried out by Xerox and previously described. A large number of the animals given toner developed primary lung tumors in this study [30, 31, 32, 33]. The study has been criticized for using doses exceeding lung-overload thresholds, and for not providing a valid basis for predicting human lung cancer risk[34]. Overloading the lungs of rats with various inert dust particles has been shown to cause increases in lung inflammation, leading to the development of lung tumors. The "19-dust study" did not include lower doses. In addition, occupational studies of workers in dusty trades (e.g. coal miners and underground miners) do not substantiate the tumorigenicity that was observed in the "19-dust study" [34,35,36,37].

Epidemiologic studies of humans exposed to toner are limited in number. There are several morbidity studies ongoing at this time. One cross-sectional study, compared "non-exposed workers" to "toner-exposed male workers" engaged in toner manufacturing, machine development, production and maintenance and recycle process. The study found no significant differences in pulmonary function between the exposed versus control groups[38] but did find a higher prevalence of respiratory symptoms (coughing and sputum) in the exposed workers compared to the non-exposed workers. However, this tendency did not exceed that of the general population [39]. Another cross-sectional study of workers handling toner dusts (toner production, machine development and machine maintenance) showed no significant reduction in pulmonary function or increased frequency of chest x-ray abnormalities or respiratory symptoms associated with exposure to toner compared to controls. However, subjects handling toner for more than 20 years showed a significantly higher prevalence of minimal chest x-ray abnormalities and lower pulmonary function values; but the number of employees in this group was small (n=27) compared to the other groups[40]. Xerox has conducted its own morbidity study since the early 1980's in toner manufacturing workers and customer service engineers (CSEs). Up to this point, serial cross-sectional analyses have been conducted. In the 1992-1996 analysis, the study found that there was no consistent pattern of work-related effects on lung function or respiratory symptoms related to exposure to toner[41].

Other studies on toner in humans include a repeated-insult patch test that found no skin irritation or sensitization reactions using Xerox toners[13]. A case-control study found an association between ever using a photocopier and sarcoidosis in African Americans. This study, based on a relatively small study population (181 sibships of which one or more had a history of sarcoidosis), relied on self-reported subject exposure and therefore would be vulnerable to recall bias [42]. There have been various case reports of adverse health effects such as occupational asthma and allergic rhinitis[43], papillitis[44], siderosilicosis[45], granulomatous pneumonitis and mediastinal lymphadenopathy[46], vocal cord dysfunction[47], and allergic eye reaction[48] associated with toner or photocopying or the toner cartridge recycling industry[49].

Since photocopiers and printers are commonly found in office environments, the effect of photocopiers/printers on indoor air quality has also received attention in recent years. Results from various studies on photocopier operators have been mixed. Photocopier operators would be exposed not only to toner and paper dust but also to the emissions from the photocopier which can include ozone and volatile organic compounds (VOC). A cross-sectional study examined respiratory symptoms in a group of photocopier workers in Taiwan. The exposed workers were located at high-volume photocopy centers; whereas controls were workers from optical stores. Although the adjusted odds ratios for respiratory symptoms were generally higher in the photocopier workers, they were not significantly different from the optical workers[50]. A study of 12 photocopier machine operators working on average 8-9 hours per day for at least 5 years revealed a significant increase in the incidence of chromosomal aberrations but no significant differences in sister chromatid exchange frequencies compared with the controls[51]. Another small study in individuals working with photocopying machines found a significant increase in basal DNA damage and a decrease in the repair efficiency in the exposed group compared to the control group using the comet assay[52]. A study on 98 photocopier operators who worked for at least 1 year showed a significant increase in the frequency of micronuclei in buccal epithelial cells and peripheral blood lymphocytes as well as chromosomal aberrations in the exposed workers as compared to 90 matched controls from different professions[53]. All three of these studies were relatively small and had no supporting exposure data.

In the 1980's, Xerox Corporation initiated a retrospective cohort mortality study in order to identify if there were any potential adverse health effects among its workers that might be associated with inhalation of toner particles. The mortality study consists of 34,147 U.S. Industrial Staff (i.e., manufacturing) and Service Engineers employed between 1960 and 1982 with the objective of evaluating any possible association between all-cause and cause-specific mortality and occupational toner exposure among Xerox employees. In the retrospective cohort design, a group is identified using historical records, (e.g., employment records) and then their survival experience is tracked using various resources that provide information on vital status. The cohort investigated in this report was established in the 1980's and vital status was previously tracked through December 31, 1984 (870 deaths), December 31, 1993 (2023 deaths) and December 31, 1999 (3374 deaths). The current analysis extends the study, tracking vital status through December 31, 2006 and thus adding an additional seven years and 2050 deaths.

Previous analyses of this mortality study have shown all-cause mortality rates of the toner-exposed Xerox workers to be lower than the general population thus consistent with the "healthy worker effect" that would be expected to get in a working population [54,55,56]. There was no evidence that toner increased all-cause mortality or mortality from all cancers, lung cancer, respiratory disease or cardiovascular disease. Standardized mortality ratios (SMRs) for the toner-exposed populations (vital status tracked through December 31, 1999) were 0.65 and 0.84 for white men and women, respectively. SMRs for all cancers, lung cancer, respiratory disease and cardiovascular disease in toner-exposed males were lower than 1.0. An increase was observed in digestive cancers in the Webster, NY populations (toner-exposed and control) that was attributed to increased rates of digestive cancers seen generally in New York State. In addition, an increase in lung cancer rates was observed in control white females[57].

In the present analyses, we used Xerox cohort data updated for employment history and vital status through December 31st, 2006. We report on the observed mortality of the employees who are classified as exposed to toner compared with a group of Xerox employees who were not exposed to toner. We compared overall and cause-specific mortality rates of exposed employees with age-, sex-, race- and calendar year-adjusted mortality rates from the US population. In addition, we compared digestive cancer rates for the Xerox populations residing in Webster, New York with New York State rates to investigate potential geographical differences in the rate of digestive cancers.

METHODS

The study cohort was originally established in the early 1980's and consisted of 34,147 employees who were considered to be eligible for the study based upon the following criteria:

- The employee had worked at Xerox for at least 91 consecutive days in an exposure group between January 1, 1960 and December 31, 1982.
- The employee had to be either (1) a toner manufacturing worker employed by Xerox in Oklahoma City, OK or in Monroe County, NY; (2) another hourly employee employed by Xerox in Monroe County, NY but not identified as having workplace exposure to toner; or (3) a Customer Service Engineer employed by Xerox and based in the United States. Employees who began Xerox employment as a supervisor, foreman, or engineer were not included in the study population. Those control or toner-exposed employees promoted to these job titles after entry into follow-up were retained in the study.

In 2008, when the final data set was being prepared for analysis, it was decided that an additional 476 employees who had not worked for the requisite 91 days at Xerox in one of the exposure groups between 1960 and 1982 should be dropped from the dataset for the analysis. The final number of employees in the dataset was 33,671. This analysis tracks the vital status of these employees through the end of 2006 and updates the previous analyses that tracked vital status through the end of 1999.

The employees were categorized into one or more of the following exposure groups:

- The **Toner-Exposed group** consists of customer service engineers (CSE) who were based in the U.S. and the hourly toner-exposed manufacturing workers (TME) based in Oklahoma City, Oklahoma (OKC) or in Monroe County, NY (WEB).

- The **Control group** (or unexposed group) consists of hourly employees from Monroe County who were not involved in toner manufacturing.

- The **Unknown group** was employees that could not be categorized in regards to exposure due to the unavailability of certain records. These employees worked only in the period from 1960 through early 1966.

Participants could contribute time to both exposed and unexposed groups, if exposed time followed unexposed time.

Exposure Assessments in Toner Manufacturing Plants

"Total dust" measurements taken using a gravimetric method as part of the company's Industrial Hygiene program were used as a surrogate for toner exposure. Total dust in some areas of the plants during different time periods may have included other dusts such as free carbon black, toner resin, toner additives and cardboard dust besides actual "toner dust". In addition to actual measurements, a concerted effort was made by a team of knowledgeable personnel to estimate dust levels prior to 1975. These estimates were based upon engineering changes in the plants, descriptions of equipment and processes when the plants opened, employee interviews, levels of production and other factors identified that might influence dust generation.

Exposure Assessments in Customer Service Engineers

Customer Service Engineers are exposed to toner during the routine maintenance and repair of copiers in customer facilities. CSEs install and relocate machines, and perform routine maintenance and repairs. Routine maintenance may include pumicing, polishing or cleaning the photoreceptor, changing developer, cleaning drum module and corotrons, replacing or cleaning the toner catch tray, filter bags or cartridges, cleaning the fuser, adding fuser oil, cleaning wick and/or downloading software. CSE's jobs tend to be highly variable depending upon the type of machine they work on, the condition of the machine, the machine location (ventilation) and the machine problems which they encounter on a day-to-day basis.

A study was undertaken in 1982 to evaluate exposures of CSEs to dust. The study was designed in 3 phases. Phase 1 consisted of monitoring under controlled environmental conditions (closed doors and HVAC systems turned off). Phase 2 (field testing) monitored 15-20 CSEs throughout the day as they did routine cleaning and maintenance of machines. Phase 3 simulated a "worst-case" scenario with CSEs cleaning the dirtiest machines available at a refurbishing center. Measurements were made using a gravimetric method [58].

Exposure Classification

Employees were categorized into exposure groups using algorithms to determine whether or not they worked in a toner-exposed job on each day that they worked at Xerox. Algorithms consisted of job codes that were considered to be toner-exposed; building numbers where toner manufacturing took place; and budget centers involved in toner manufacturing. The algorithms were updated as job codes, building and budget centers changed.

At the beginning of the study, work history records were constructed for all employees working in the supplies organization at the end of 1982. In addition, detailed work history was constructed for all employees who had been identified as toner-exposed. Exposure for the period through the end of 1982 was based on various employee records including IRS941A wage lists, job history, union cards and medical records.

For all subsequent analyses, the information for the original cohort members was updated with additional exposure information (budget center numbers, job codes and building numbers) and employment status taken from an electronic employee database. Control time was calculated as any time spent as a union employee that had not been assigned to toner-exposed time. Examples of the types of jobs that were counted toward control time are maintenance (carpenters, welders, electricians, groundskeeper, machinists, maintenance engineers, truck drivers, painters, pipe fitters), fork truck operators, assembly, machine rebuilders, photoreceptor manufacturer, press operators, receiving clerks, riggers, stock handlers and cleaners, if not assigned to the toner manufacturing facility.

This analysis updated exposure status through the end of 2006. Time at risk was apportioned to the appropriate exposure group once an individual had been working in a given capacity for 91 days. Follow-up began three months after an employee entered a specific exposure group or January 1, 1960, whichever was later. For controls who became toner-exposed, end of follow-up as a control is the date of first toner exposure minus one day. For toner-exposed workers who moved to non-toner jobs, subsequent years of follow-up were assigned to the toner-exposed group.

Vital Status and Cause of Death

Vital status through December 31st 2006 was ascertained through the National Death Index and/or the Social Security Master Death File with cause of death obtained through NDI Plus services, or death certificates requested from the States or from Xerox Benefit group records. Causes of death were reported as either International Classification of Diseases, version 9 (ICD9) or version 10 (ICD10) codes with the later converted to ICD9 before analysis. Individuals not reported dead were assumed to be alive up to the end of ascertainment. No attempt was made to obtain death certificates from foreign countries. In addition, an agreement was not in place with New York City to obtain death certificates for persons dying there. Notice of these deaths was often obtained through other sources (e.g., Xerox Benefits or SSA) but cause of death could sometimes not be obtained. In these cases, the deaths were included under "all-cause" but were not included in any cause-specific mortality analysis. For controls who became exposed but did not contribute sufficient follow-up time to contribute to the exposure category (<91days in a toner-exposed capacity), subsequent deaths were ignored (censored) and did not contribute to counts for either control or exposed groups.

SMR Analysis

To examine the association between toner exposure and various demographic characteristics of the Xerox cohort, employees were stratified by gender (male, female), race (white, non-white) and exposure (exposed, unexposed). Given the high proportion of white and male employees among those with known race and gender, those with missing race were assumed to be white and those with missing gender information were assumed to be male. Subgroups of exposure based on employment capacity (TME, CSE) and location of employment (OKC, WEB) were also examined. The distribution of deaths among categories defined by these demographic factors and exposure was evaluated and crude estimates of the incidence rate of all-cause mortality were calculated. The overall survival experience of the controls and exposed employees was described using Kaplan-

Meier survival function estimates. The effect of age on mortality was accounted for by using age as the time axis for assessing survival. Thus, the survival in the exposed and unexposed could be compared for employees of equivalent ages.

Using estimates of the cause-specific mortality rate from the US population for 23 categories of causes of death, we computed standardized mortality ratios (SMRs) adjusted for age, sex, race and calendar year. Reference mortality rates for the period of 1979 through 2006 were obtained from the Centers for Disease Control (CDC) using the CDC Wonder mortality statistics request system[59]. Reference mortality rates for the period of 1960 though 1978 were obtained using the tabulated data files from National Center for Health Statistics (NCHS)[59]. For 10 specific cancer diagnoses (esophagus, stomach, colon, rectum, liver, pancreas, prostate, testis, kidney and bladder) rates were not available for the years 1960-1978. Rates for the 10 cancer categories were interpolated for those years using the proportional change in the rate for the most related available cancer category. Confidence intervals were calculated based upon exact Poisson probabilities using the method of Breslow and Day[60]. The categories of cause of death were chosen to mirror previous reports from the Xerox Mortality Study. A listing of the International Classification of Diseases, version 9 and version 10 codes, used to group causes is given in Appendix A. The SMR analysis provided a standardized external comparison for evaluating whether the rate of death from various causes in the Xerox cohort was higher or lower than that expected for the US population. Any SMR based on 5 deaths or less was not reported due to the instability of the estimate[i]. However, the number of observed and expected deaths in these cases was reported.

No adjustments were made for multiple comparisons in the calculation of the confidence intervals (calculated to provide nominal 95% coverage of the true value as per standard frequentist statistical theory). In other words, because multiple tests of statistical significance were carried out, there is the possibility that some associations arose by chance alone. However, we note that for our SMR calculations, we computed confidence intervals for 23 SMR analyses (for all-cause, all-cancer, and individual cause-specific mortality outcomes) for 28 different groups and subgroups (defined by sex-, race-, exposure-, and location-criteria). A conservative approach for evaluating the evidence for any SMR estimate being statistically different from 1.0 is a Bonferroni correction that would require testing each at a $0.05/644 = 7.7 \times 10^{-5}$ level. We chose to use less stringent criteria, applying an alternative method for controlling the overall *false-discovery rate* (FDR). The Benjamini-Hochberg (B-H) approach accomplishes control of the FDR by comparing the observed pvalue in sequential order (from largest to smallest) to a list of critical values. The first value is the overall

[i] In cases for which there were less than 5 deaths in the race/gender/exposure group, the SMR was not calculated due to the instability of the SMR with that small a sample. The National Center for Health Statistics does not publish or release rates based on fewer than 20 observations, because they feel these data do not meet their requirement for a minimum degree of accuracy. They base the accuracy requirement on a measure called the relative standard error (RSE). The RSE is the standard error as a percent of the measure itself. http://www.health.state.ny.us/diseases/chronic/ratesmall.htm

Type I error rate ($\alpha/2$ for two-sided testing); the last value is the Bonferroni critical value and all of the other pvalues are compared to statistical thresholds between the two values. We utilized this approach in evaluating the statistical significance of the 644 SMR values.

Sensitivity Analyses

Two additional analyses were performed to assess the degree to which the assumptions that were made affected the SMR estimates. For the assumption concerning pre-1979 cancer rates, the SMR analysis was rerun using only person-time and events after 1979. For assumption of employees with unknown race being white and unknown gender being male, the SMR analysis was rerun leaving these employees out.

Data Handling

All data were kept at Xerox in a secure environment. All electronic data were encrypted. Access to the records was limited to authorized staff on a need-to-know basis. Data were used only for research and statistical purposes. No data will be published or released in any form where a particular individual is identifiable.

Once data collection was determined to be complete, an electronic file was prepared (stripped of all identifiers) and sent to Johns Hopkins Bloomberg School of Public Health for analysis. For additional details on the study methodology refer to the study protocol, *The Retrospective Cohort Study of Mortality of Xerox Employees (Vital Status Tracked through December 31, 2006)*, authorized January 15, 2010 [61].

The study was reviewed and approved by the Western Institutional Review Board. Approvals were also obtained from various State Institutional Review Boards (IRB), Human Investigation Committee, or Human Subjects Review Boards as a requirement for requesting death certificates from these individual states.

RESULTS

Demographics of the Cohort

The study cohort consisted of 33,671 employees. Of these employees, information on dates of birth was unavailable for 1,705 (5 %). Since participant age is necessary for calculating SMRs, the employees with missing dates of birth were excluded from the study cohort for the purposes of this analysis leaving 31,966 employees. Table 1 presents the descriptive statistics on the eligible versus the excluded population. Since the majority of the excluded employees was also missing information on race (99.5 %) and gender (96.7 %), a statistical comparison of the demographics between the two populations was not possible.

Table 1. Comparison of the eligible population to the employees excluded for unknown dates of birth

	Eligible		Excluded	
	Number	%	Number	%
Non-White	5,461	17.1	3	0.2
White	21,288	66.6	5	0.3
Unknown Race	5,217	16.3	1,697	99.5
Control+Exposed	566	1.8	1	0.1
Control	9,990	31.3	304	17.8
Exposed	20,943	65.5	297	17.4
Unknown Exposure	467	1.5	1,103	64.7
Male	28,113	87.9	52	3.0
Female	3,691	11.5	5	0.3
Unknown Gender	162	0.5	1,648	96.7
Total	31,966		1,705	

Of the 31,966 remaining members of the study cohort, 88 % were male and 67 % were white. Race was not known for 5,217 employees (16 %) and for the purposes of the primary analysis these employees were assumed to be white. Gender was not known for 162 employees (1 %) and these were assumed to be male for the purposes of the primary analysis.

Table 2 presents descriptive statistics for the cohort stratified by race and gender. The numbers of non-white females (745) and white females (2446) in the cohort were relatively small with 86 and 579 deaths, respectively. Therefore interpretation of cause-specific SMRs for the smaller female subgroups was difficult due to wide confidence limits.

Table 2. Distribution of the eligible employees by race and gender							
RACE	Male		Female		Unknown		Total
	Number	%	Number	%	Number	%	Number
Non-White	4,714	16.8	745	20.2	2	1.2	5,461
White	18,841	67.0	2,446	66.3	1	0.6	21,288
Unknown	4,558	16.2	500	13.5	159	98.1	5,217
Total	28,113		3,691		162		31,966

The median age at entry into the cohort was 25 years with an interquartile range (IQR) (25^{th} and 75^{th} percentile) of 22 to 28 years. The median follow-up time was 33 years (IQR 28-38). The 31,966 cohort members accrued a total of 1,053,145 person-years of observation during the 46-year observation period.

There was a total of 5,424 deaths (17 % of the population) identified during the 46-year observation period. The remaining members of the cohort (26,542) were assumed to be alive. Approximately 3400 employees were still actively working at Xerox on January 1, 2007.

For 128 deceased employees, the underlying cause of death could not be determined but the dates of death were known. The majority of these deaths occurred in New York City or a foreign country or were deaths based on SSA evidence only and the death certificates could not be obtained. These deaths were included for "all-cause mortality" but were not included in any cause-specific mortality analyses.

Exposure Groups

Table 3 presents the distribution of employees by gender/race for each exposure group. There were 21,509 members of the cohort (67 %) exposed to toner and 10, 556 controls (33 %) who were manufacturing workers not exposed to toner. For 467 members of the cohort (1 %), there was insufficient information available to categorize their exposures and they were placed in an unknown exposure group.

Table 3. Distribution of race, sex and exposure among the eligible employees									
	White Male		Non-White Male		White Female		Non-White Female		Total
	#	%	#	%	#	%	#	%	#
Exposed	16,080	74.8	3,936	18.3	1,165	5.4	328	1.5	21,509
CSE	15,465	75.0	3,798	18.4	1,073	5.2	278	1.3	20,614
TME	619	68.8	139	15.4	92	10.2	50	5.6	900
-OKC	93	62.0	29	19.3	16	10.7	12	8.0	150
-WEB	527	70.2	110	14.6	76	10.1	38	5.1	751
Control	7,522	71.3	861	8.2	1,728	16.4	445	4.2	10,556
Unknown	344	73.7	5	1.1	113	24.2	5	1.1	467
Overall	23,559	73.7	4,716	14.8	2,946	9.2	745	2.3	31,966

Approximately 96 % of the exposed population were CSEs. The group involved in toner manufacturing (TME) was small, consisting of 900 cohort members divided between two sites: Oklahoma City (OKC) and Webster (WEB).

Descriptive statistics (gender, race, birth year and age of entry into cohort for each exposure group) are presented in Appendix B, Table B1. Differences in age of entry into the cohort were observed with the youngest group being those with unknown exposure with a median age of 24 years, followed by CSEs (median age of 25 years), OKC (median age 26 years), controls (median age 27 years) and lastly the WEB population (median age 29 years).

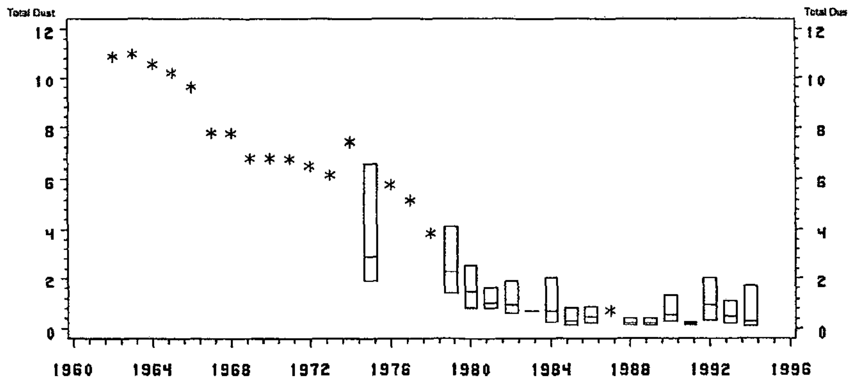
The number of deaths and the person-years of follow-up, stratified by exposure group and gender/race combinations, are presented in Appendix B, Tables B2 and B3, respectively. Crude death rates are presented in Appendix B, Table B4. The overall cohort survival estimates plotted as a function of participant age are presented in Appendix B, Figure B1; the curves show that the survival experience of the overall exposed group is slightly better across all ages compared to that of the control group.

Exposure Assessment

As part of the industrial hygiene program at Xerox, dust levels have been measured in the plants as a surrogate for toner exposure. Approximately 610 and 756 personal air-monitoring measures were available from the Oklahoma City and the Webster plants, respectively, between 1975 and 1994. Respirable dust measurement (TWA) were begun at the OKC (n=438) and the WEB plants (n=617) in the late 1980's.

Dust levels in Webster toner manufacturing plants have declined substantially over the years to less than 1 $^{mg}/_{m3}$ currently, much lower than the current exposure limit of 15 $^{mg}/_{m3}$ for total dust set by the US government (OSHA). In fact, estimated mean total dust levels have always been below this limit, dating back to the 1960's. The median respirable dust levels since the late 1980s is approximately ~0.05 $^{mg}/_{m3}$. Figure 1 shows total dust levels (median and interquartile range) in the Webster Plants. Estimates of mean total levels of dust in the plants are denoted by stars.

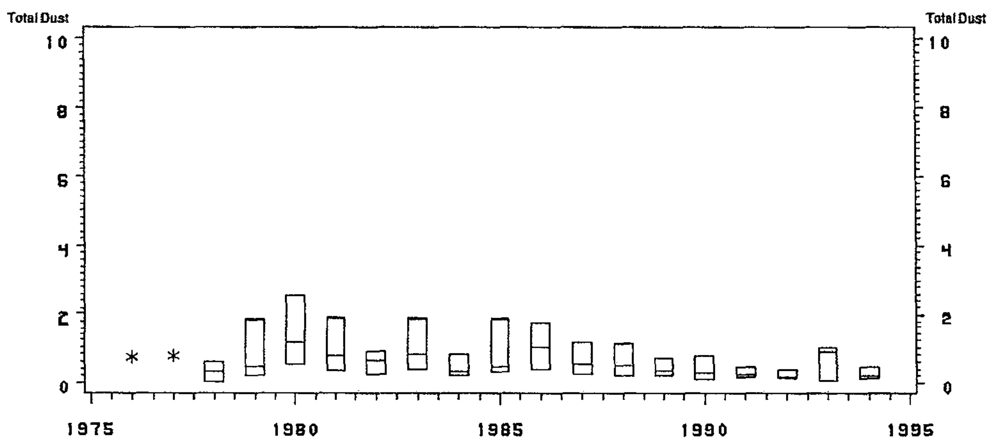
Webster Toner Plant
Historical Total Dust Exposures (mg/m3)



Note: Boxes denote the interquartile range (IQR); the line is the median; stars represent estimated means for years when no data was available

Levels at the OKC plant have been fairly low since the plant opened in 1976. The median respirable dust level in the late 1980s and early 1990s was ~0.05 $^{mg}/_{m3}$. Figure 2 show total dust levels (median and interquartile range) in the OKC Plant from when it opened in 1976 until 1994.

Oklahoma City Toner Plant, OK
Historical Total Dust Exposures (mg/m3)



Note: Boxes denote the interquartile range (IQR); the line is the median; stars represent estimated means for years when no data was available

Dust levels between 2002-2007 at the OKC plant were even lower with 12 out of 73 total dust samples in the toner operations being below the limit of detection; and the median of the remaining samples being 0.10 $^{mg}/_{m3}$. For respirable dust, 41 of 76 were below the level of detection and the median of the remaining samples was 0.03 $^{mg}/_{m3}$.

Levels in the resin areas were slightly higher (2 of 33 total dust samples were below limit of detection; median of 0.25 $^{mg}/_{m3}$; 9 of 29 respirable dust were below the limit of detection; median level of 0.05 $^{mg}/_{m3}$) but still every low[62] .

Dust exposures for CSEs to airborne toner are typically lower than in the manufacturing plants and tend to be highly variable day-to-day depending upon type and condition of machine and the room ventilation and the specific repair task. Results from the controlled testing (worst-case ventilation conditions: closed doors and HVAC system turned off) of exposures received by CSEs indicated that TWA total dust concentrations ranged from below the limit of detection up to 0.34 $^{mg}/_{m3}$.. Results of field testing measured TWA total dust concentrations ranging from 0.09 to 0.94 $^{mg}/_{m3}$ with an average of 0.28 $^{mg}/_{m3}$. One higher value (3.0 $^{mg}/_{m3}$) was considered to be suspect and was rejected. The average TWA concentration for total dust measured during worst case testing was only slightly higher (0.38 $^{mg}/_{m3}$)[58].

SMR Analysis- all-cause

The SMRs (based on US rates), 95 % confidence limits, and the expected and observed numbers of deaths by exposure groups for each race/gender group are presented in Appendix C for 23 causes of death categories.

The SMRs and their 95 % confidence limits for all causes of death by exposure group and gender/race category are presented below.

SMR for "ALL CAUSES" of death with 95% confidence limits				
Exposure Group	**White Male**	**NW Male**	**White Female**	**NW Female**
Eligible	0.75* (0.73, 0.77)	0.50* (0.46, 0.54)	0.88* (0.81, 0.96)	0.72* (0.58, 0.89)
Exposed	0.64* (0.61, 0.67)	0.43* (0.39, 0.47)	0.78* (0.61, 0.99)	0.59* (0.35, 0.93)
CSE	0.63* (0.6, 0.66)	0.42* (0.38, 0.46)	0.87 (0.67, 1.12)	0.63 (0.35, 1.04)
TME	0.85 (0.7, 1.03)	0.86 (0.56, 1.25)	0.44* (0.19, 0.87)	Less than 5 deaths
OKC	1.24 (0.69, 2.04)	1.32 (0.57, 2.6)	No deaths	Less than 5 deaths
WEB	0.81 (0.65, 1.00)	0.74 (0.44, 1.17)	0.48* (0.21, 0.94)	No deaths
Controls	0.87* (0.83, 0.91)	0.72* (0.63, 0.83)	0.92 (0.84, 1.00)	0.77* (0.6, 0.98)
Unknown	0.83 (0.68, 1)	Less than 5 deaths	0.48* (0.28, 0.79)	Less than 5 deaths

For groups which had at least 5 deaths, the SMRs for all causes of death were below 1.0 for all groups or included 1.0 in the 95 % confidence limits as was the case for OKC males (white and non-white). In many of the groups, especially the larger ones, the SMRs were statistically significantly decreased (indicated with an ' * ') compared to the US population. Thus, the mortality experienced by each of these groups was no different (if not slightly better) than the mortality expected from the general population. This was anticipated given the well described phenomenon of the "healthy worker effect" [63,64].

SMR Analysis (all cancers, lung cancer, respiratory and cardiovascular disease and diabetes)

Similar results were observed with mortality from all cancers, lung cancer, respiratory and cardiovascular disease and diabetes in white males, conditions for which an increase in mortality due to exposure to particulate matter could be hypothesized. The table below shows the SMRs for white males, for the toner-exposed, CSE, TME and control groups for the outcomes of all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes. Echoing the previous findings, these SMRs are generally lower than 1.0 or include 1.0 in the confidence limits, indicating no differences from the general population for white males.

SMRs with 95% confidence limits for WHITE MALES					
Exposure Group	**All Cancers**	**Lung Cancer**	**Respiratory Disease**	**Cardiovascular Disease**	**Diabetes**
Exposed (N=16,080)	0.76* (0.7, 0.82)	0.65* (0.56, 0.75)	0.51* (0.39, 0.65)	0.62* (0.57, 0.67)	0.51* (0.36, 0.70)
CSE (N=15,465)	0.75* (0.69, 0.81)	0.63* (0.54, 0.73)	0.49* (0.37, 0.63)	0.61* (0.56, 0.66)	0.50* (0.35, 0.70)
TME (N=619)	1.09 (0.76, 1.52)	1.17 (0.63, 2.01)	5 deaths	0.87 (0.61, 1.21)	0.69 (0.08, 2.48)
Controls (N=7522)	1.01 (0.93, 1.09)	0.98 (0.85, 1.12)	0.79* (0.65, 0.95)	0.83* (0.77, 0.89)	0.68* (0.48, 0.94)

Looking only at the exposed population (CSE and TME combined), the table below presents the SMRs for each race/gender group. Results are again similar with statistically significant decreases observed compared to the general population for white and non-white males for all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes. The number of females in this group was relatively small resulting in wider 95% confidence limits.

SMRs for EXPOSED GROUP (CSE and TME combined) with 95% CLs					
Gender/ Race	**All Cancer**	**Lung Cancer**	**Respiratory Disease**	**Cardiovascular Disease**	**Diabetes**
WM N=16,080	0.76* (0.70, 0.82)	0.65* (0.56, 0.75)	0.51* (0.39, 0.65)	0.62* (0.57, 0.67)	0.51* (0.36, 0.70)
NWM N=3,936	0.55* (0.45, 0.67)	0.45* (0.30, 0.65)	0.37* (0.17, 0.70)	0.45* (0.37, 0.53)	0.48* (0.25, 0.81)
WF N=1,165	1.02 (0.70, 1.43)	0.68 (0.22, 1.58)	Less than 5 deaths	0.28* (0.10, 0.61)	No deaths
NWF N=328	0.94 (0.41, 1.85)	Less than 5 deaths	Less than 5 deaths	Less than 5 deaths	No deaths

SMR analysis- other findings

Overall in this analysis, SMRs were calculated for 23 categories of death for each race/gender/exposure group for which there was more than 5 deaths. Across the various strata, statistically significant increases (denoted by *) in the SMRs were observed for the following:

STATISTICALLY SIGNIFICANT INCREASES IN SMRS		
Breast Cancer	Exposed White Females N=1,165	1.86* (1.02, 3.12)
	White Female CSEs N=1,073	2.17* (1.18, 3.63)
Lung Cancer	Eligible White Females N=2,946	1.54* (1.21, 1.94)
	White Female Controls N=1,728	1.75* (1.36, 2.22)
Stomach Cancer	White Male Control N=7,522	1.63* (1.09, 2.36)
Rectal Cancer	White Male Control N=7,522	1.85* (1.06, 3.0)

The statistically significant increase (SMR=2.17) observed in breast cancer in white female CSEs was not observed in non-white CSE females (2 deaths observed; 1.8 expected) and there were no deaths due to breast cancer in the TME group (WF and NWF) which would be expected to be the group with the highest exposure level.

A statistically significant increase was observed in lung cancers in the white female controls; that was also observed in the previous follow-up of this cohort. The SMR for lung cancer (white female controls) was 1.75 (95% CL 1.36, 2.22) for the current analysis compared to 1.63 (95% CL 1.16, 2.22) for the previous follow-up. There were 67 deaths due to lung cancer in the white female control group (n= 1,728); the expected number of deaths was 38. The Benjamini-Hochberg (B-H) approach was used to control the overall *false-discovery rate* (FDR), potentially inflated as a result of the 644 significance tests that were performed on the data. The SMR for lung cancer in the white female controls was the only SMR remaining significant after the more stringent significance criterion was applied. This increase in lung cancer incidence was not seen in other race/gender control categories; the SMRs for white males controls, non-white male controls and non-white female controls were 0.98 (95% CL 0.85-1.12), 0.71 (95% CL 0.40-1.15) and 0.62 (95% CL 0.13-1.81), respectively.

Statistically significant increases in stomach and rectal cancers were observed in the white male control group, as in the previous follow-up. The table below presents the SMRs for the current analysis and the two previous follow-ups that tracked vital status through the end of 1993 and 1999, respectively.

SMRs with 95% Confidence Limits in WHITE MALES CONTROLS (N=7,522)			
	Previous analysis with vital status tracked thru 12/31/93	Previous analysis with vital status tracked thru 12/31/99	Current Analysis Vital status tracked thru 12/31/06
Digestive CA	1.19 (0.95, 1.48)	1.24* (1.03, 1.48)	1.09 (0.93, 1.27)
Stomach CA	1.80* (1.05, 2.89)	1.71* (1.06, 2.61)	1.63* (1.09, 2.36)
Rectal CA	1.66 (0.76, 3.14)	2.22* (1.18, 3.80)	1.85* (1.06, 3.00)

Historically, the rates of digestive cancers have been higher in NYS compared to US rates. Because of this geographical distribution, the digestive cancers (stomach and rectal) in this study were further investigated by calculating SMRs using New York State rates obtained from the CDC[59]. These SMRs are presented in Appendix D. SMRs calculated using the higher NYS rates for the reference population, although still above 1.0 for stomach and rectal cancers, were no longer statistically significant.

SMRs with 95% Confidence Limits for WHITE MALE CONTROLS (N=7,522)		
	SMRs derived from NYS rates	**SMRs derived from US rates**
Esophagus Cancer	1.21 (0.79, 1.79)	1.26 (0.81, 1.86)
Stomach Cancer	1.36 (0.90, 1.96)	1.63* (1.09, 2.36)
Colon Cancer	0.94 (0.71, 1.23)	1.03 (0.78, 1.35)
Rectal Cancer	1.68 (0.96, 2.73)	1.85* (1.06, 3.00)
Digestive Cancers	1.01 (0.86, 1.17)	1.09 (0.93, 1.27)

A statistically significant increase in all cancers (SMR =3.16; 1.03, 7.38) was seen in the previous analysis in white males at the Oklahoma City Plant. The SMR (SMR=2.34; 95 % CL 0.94, 4.83) in the current analysis is still above 1.0; however, the confidence limits now include 1.0. The number of deaths (7) is still relatively small.

Sensitivity Analyses

The sensitivity analysis with removal of employees for which we had no race or gender is shown below for the toner-exposed population for all causes, all cancers, lung cancer, respiratory and cardiovascular disease and all external causes.

ORIGINAL ANALYSES COMPARED TO SENSITIVITY ANALYSIS (EMPLOYEES WITH UNKNOWN RACE AND GENDER EXCLUDED FROM ANALYSIS)

				95% Confidence Limits		
CAUSE OF DEATH	Observed Deaths	Expected Deaths	Person Years of Follow-up	Lower Limit	Upper Limit	SMR
All cancer[ii]	751	1028.13	699424.96	0.68	0.78	0.73
(sensitivity)[iii]	599	867.39	601018.29	0.64	0.75	0.69
All causes	2391	4030.17	699424.96	0.57	0.62	0.59
(sensitivity)	1855	3450.97	601018.29	0.51	0.56	0.54
All external	309	613.06	699424.96	0.45	0.56	0.50
(sensitivity)	213	535.58	601018.29	0.35	0.45	0.40
Ca lung	215	346.05	699424.96	0.54	0.71	0.62
(sensitivity)	174	289.89	601018.29	0.51	0.70	0.60
Cardiovascular disease	717	1254.89	699424.96	0.53	0.61	0.57
(sensitivity)	562	1064.42	601018.29	0.49	0.57	0.53
Respiratory disease	77	154.62	699424.96	0.39	0.62	0.50
(sensitivity)	67	129.14	601018.29	0.40	0.66	0.52

For the most part, differences between the two analyses were small and confidence limits overlapped.

Similarly, removing the person-time prior to 1979 did not result in any changes in the SMRs for those outcomes that had imputed rates.

DISCUSSION

Printers and photocopiers that use toner are widespread in our society. As the company that introduced toners into wide commercial use, Xerox has taken a responsibility to understand the biological effects of toner. In the 1980s, Xerox started a series of three studies to investigate the possible health effects of toners. The first was an inhalation study in animals; the second a morbidity study of Xerox employees exposed to toner; and the third, a mortality study of a cohort of Xerox employees. This report discusses the results from the ongoing mortality study. To the best of our knowledge, this study of approximately 34,000 employees is the only study examining mortality in a cohort of workers exposed to toner. The cohort has now been followed for up to 47 years; and 17 % of the cohort has died.

The two groups of exposed workers in this study are toner manufacturing workers, and customer service engineers. Dust measurements were used as a surrogate for

ii Original analysis assuming employees with unknown race were white; and unknown gender were male.
iii Sensitivity analysis excluding those employees with unknown gender and/or race.

toner exposure in this study. The Webster toner manufacturing workers were exposed to median levels of total dust estimated to be in the range of 10-12 $^{mg}/_{m3}$ from toner and raw materials early in the study (1960's). These levels dropped gradually as engineering changes were put into place to lower them. Current levels are below 1 $^{mg}/_{m3}$. Total dust levels at OKC were never as high (median levels < 2 $^{mg}/_{m3}$). Customer service engineers are exposed to lower levels of dust but higher than what customers would be exposed to. Customers can be exposed to dust through machine emissions. Dust associated with copying and printing consists primarily of paper particles and fibers, with smaller amounts of toner particles (<20 %). Typical airborne concentrations of total dust measured at the operator's position of various Xerox equipment ranged from 0.002 to 0.025 for office equipment; and 0.03 to 0.07 for production equipment[10].

Previous reports from this ongoing "Xerox Mortality Study" have suggested that toner exposure in this cohort does not increase the risk of mortality overall or in any of the disease categories evaluated. This report, using data updated for vital statistics through December 31st, 2006, supports previous results. In general, there was a pattern of lower mortality in the Xerox population than expected compared to US mortality rates. The SMR for all causes was 0.64 for the white male exposed populations; 0.78 for white female exposed population; 0.43 for non-white exposed males; and 0.59 for non-white exposed females. In addition, the SMRs for all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes in white and non-white males were all lower than 1.0 in the toner-exposed population with confidence limits not including 1.0. This pattern of generally low SMRs suggests that exposure to toner in an occupational setting does not cause an increase in mortality due to cancer, lung cancer, respiratory disease, cardiovascular disease or diabetes. All of these are conditions for which, an increase due to exposure to particulates might be hypothesized.

The finding that the majority of the SMR estimates were below 1.0 for the Xerox population is consistent with the "healthy worker effect" (HWE) typically observed in occupational cohort studies[63]. The healthy worker effect is the phenomenon whereby workers typically have overall death rates lower than those in the general population, due to selection factors in the working population and to employment-associated benefits such as economic factors, health insurance and lifestyle changes. The HWE tends to be stronger for all-cause mortality than for mortality due to cancer, possibly due to the disease (cancer) not being readily apparent or present at the time of hire[63,64].

The two most common causes of death in the Xerox population were cardiovascular disease and cancer, mirroring the leading causes of death in the US population for 2005[65], 2006[66] and 2007[67].

Previous follow-ups of this cohort found an increase in digestive cancers in both the white male control and toner-exposed populations in Webster, NY; an increase in lung cancer in white female controls; an increase in prostate cancer in the TME non-white males; and an increase in all cancers in white OKC males. The higher rate of digestive cancers observed in previous follow-ups in the Webster populations (control and toner-exposed) was thought to be a consequence of the choice of the reference rate (national versus state-specific). SMRs for the white male control population in the current analysis were 1.26 for esophagus; 1.63 for stomach; 1.03 for colon; 1.85 for rectum; and 1.09 for digestive cancers, with the increases being statistically significant only for stomach and rectal cancer, when compared to the US population. When compared to New York State rates, the SMRs were decreased to 1.21, 1.36, 0.94, 1.68 and 1.01 for esophageal, stomach, colon, rectal and digestive cancers, respectively, in white male controls and the respective 95 % confidence limits all included one. The rate of digestive cancers in white male Webster toner manufacturing population was also above 1 (SMR of 1.41 when compared to the US population and a SMR of 1.3 compared to NYS rates); however, the 95 % confidence limits included one in both cases. SMR estimates for site-specific digestive cancers in the Webster toner manufacturing population were hampered by small numbers.

Therefore, the increase in digestive cancers observed in the Webster control white male population may be attributable in part, to the choice of reference rates (national versus state-specific) that do not adequately reflect the higher mortality rates from these cancers in the local population. However, even when NYS rates are used as the reference, the SMRs, although no longer statistically significant, are still greater than 1.0. Known risk factors for stomach cancer include *helicobacter pylori* infection, family history, dietary factors and smoking. Some reports in the literature have shown dusty occupations to be associated with increases in gastric cancers and have suggested that dusts when swallowed might play a co-carcinogenic role acting as an irritant to the gastric mucosa[68, 69]. However, since in this study the increase in stomach cancer was observed in the white male control group, these reports in the literature are not relevant to explaining this excess.

A case-control study was conducted following the initial analysis of the Xerox mortality data, to evaluate the association of job category by seniority unit with deaths due to digestive cancers in the control group. Seniority unit was used since classification by job category produced numbers too small to allow statistical analysis and many work histories by specific job category were incomplete. In this previous analysis, there were 46 deaths due to digestive cancer when approximately 35 would have been expected based on reference rates. The excess consisted of cancers of the stomach and esophagus. A statistically significant association was not found between seniority unit and death due to digestive cancer. However, the proportion of deaths in the cleaner seniority unit was consistently higher for cases then for controls. Among the 8 cleaners, who died of stomach/esophagus cancers, 6 were foreign-born. The study report concluded that there appeared to be selection factors (country of birth) operational that were associated with increased mortality due to digestive cancer in the cleaner seniority unit[70].

Therefore, we were interested in examining the relationship between country of birth and stomach cancer in the current analysis. Unfortunately, due to changes in how we collect the death certificate information, we no longer receive country of birth information for all deaths . However, of the 28 observed deaths due to stomach cancer, we have country of birth for 20 and of these 10 were foreign-born (6 from the Ukraine, and 1 each from Poland, Italy, Netherlands and Greece).

Numerous reports in the scientific literature link differences in mortality rates to country of birth. A study done in Buffalo, NY on ethnic derivation as it relates to cancer at various sites, concluded that foreign-born males had a 2.5 times higher risk for gastric cancer and 2.1 higher risk for esophageal cancer than native-born men[71]. Another study, looked only at people living in New York State (exclusive of NYC), and compared death rates due to cancer among the foreign-born compared to white native-born residents of NYS during the years 1969 to 1971. All of the ethnic groups studied showed elevated gastric cancer risks when compared to white native-born males (e.g., SMR of 2.63 for Poland; SMR of 1.95 for Italy)[72]. A third study, using data from the National Longitudinal Mortality Study (1979-1989), derived mortality risks of immigrants relative to US-born people, adjusting for age, race/ethnicity, marital status, urban/rural residence, education, occupation and family income. The study found that immigrants showed higher risks for stomach cancer.[73]. Therefore, it is possible that the selection bias that was found in the first analysis is still exerting an effect and that the excess of digestive cancers in this population is due to the proportion of foreign-born individuals in New York State as a whole; and possibly in the Xerox workforce at that time.

In the previous analysis, significant increases in mortality were found for all-cancer in the OKC white males; prostate cancer in the TME non-white males; and lung cancer in the control white females, compared to the general US population. The estimates for all cancer and prostate cancers were generated from extremely small numbers of deaths and were not consistent across race/gender groups or across exposure groups, suggesting that these findings were likely due to chance. The current results, although still based on small numbers of deaths (7 and 2 deaths, respectively), are no longer statistically significant, thus, substantiating that these increases were probably due to chance.

In contrast, the rate of lung cancer in the control white females is increased (SMR= 1.75; 95% CL 1.36, 2.22). Occupational cohort mortality studies typically lack data on smoking making it difficult to determine whether or not an excess of a smoking-related disease is the result of an occupational exposure. However, the increase in lung cancer that we are seeing in this study is in the control population suggesting no relationship to toner exposure. Previously, we hypothesized that this increase might be a result of smoking behavior, that could not be assessed in this study.

A study done by Shell Oil Company looked at the prevalence of smoking in their employee population, divided into production (hourly) versus staff (salaried) workers by gender, compared to US rates. They found the highest prevalence of smoking in women working in production (hourly) jobs during each of the 3 periods (1970's, 1980's and 1990's), they evaluated. When the rates were age-adjusted to the US population, these rates were higher than the US rates for two of the 3 periods [74]. Another study looked at smoking habits of automotive workers compared to the general population, using data from the Health Interview Surveys (HIS) conducted by

NCHS. They found that the proportion of smokers in the automotive worker population, generally exceeded those in the general population by at least 10% for most age, race and sex categories [75]. A third study using HIS data from 1970 concluded that smoking occurs with a higher prevalence among blue collar workers compared to professionals, managers or technically-trained individuals; and that smoking among women, especially white females is more prevalent among the employed than among unemployed women [76]. These studies suggest that females in production jobs tend to have a higher prevalence rate of smoking than the general US population. Therefore, although smoking data are not available in our study, we might again hypothesize that our population of control white females had a higher rate of smoking leading to the higher rates of lung cancers observed in this study.

One commonly used method to control for smoking in occupational cohort mortality studies is to analyze other smoking-related causes of death, besides the cause of death of interest [77]. Therefore, in an attempt to further investigate our hypothesis, we calculated a combined SMR for multiple cancers (esophagus, pancreas, bladder, kidney, liver and stomach) that are known to be caused by smoking to determine if that rate was also increased [78]. Combining these cancers, we would expect to see 19 deaths, instead of the 22 that were observed (SMR= 1.15; 95% CL 0.72-1.74); a non-significant, but slightly increased rate.

An increase was observed in breast cancer in white female CSEs (SMR=2.17; 95% CL 1.18, 3.63) in this study. Known risk factors for breast cancer include age, gender (female), family history of breast cancer, reproductive characteristics associated with estrogen and other hormones (e.g., age at first full-term pregnancy, early menarche, late menopause, postmenopausal obesity, use of combined estrogen and progestin menopausal hormones, recent oral contraceptive use, and no full-term pregnancies) and activities that affect hormone levels (e.g., alcohol consumption, physical inactivity).

The population of white female CSEs in this study is relatively small (n=1073). Their average age at entry into the cohort was 26 years. Forty-two percent of them worked at Xerox for 5 or less years. Seventy-seven percent of them were hired in the 1970's with only 4% hired in the 1960's. Out of the 14 deaths due to breast cancer in this group, 2 of them worked at Xerox for less than 1 year; 7 of them worked for between 1-5 years; and 5 worked for more than 5 years. Ten of the 14 were 50 years or older when they died. In short, there appeared to be no particular association between years of employment at Xerox and premature mortality due to breast cancer in this group.

Literature reviews looking at occupational risk factors[79] and/or environmental exposures[80] that might be associated with breast cancer in females have for the most part not been able to draw any definitive conclusions, due to the inherent limitations of the studies (e.g., small size/low statistical power, confounding risk factors, poor quality exposure data, and/or issues of timing with respect to latency and breast vulnerability). Confounding risk factors, such as having no children or having the first child at a late age, among others, may be more prevalent in a working population of females than in the general US population, in which a sizeable fraction of women may not work outside the home [81]. Some earlier studies reported increased risks of breast cancer in a number of female occupational groups (e.g., teachers, nurses and office clerical workers). The majority of these increases are thought to be related to parity and maternal age at first birth [82,83]. One study in particular looked at 165,912 deaths among females age 20 or older and found significantly elevated proportional mortality ratios (PMRs) for breast cancer in teachers, nurses, office clerks and sales clerks, compared to the general population. When homemakers were excluded from the general reference population, most of the excesses in risk disappeared [84].

More recent work in the field has tried to control for risk factors. One study, reported an association between nulliparity and late first childbirth with more aggressive breast cancer subgroups [85]. A case-control study, done in Canada, looked at associations of postmenopausal breast cancer with various workplace exposures, while controlling for many of the risk factors that confounded earlier studies. The study looked at 556 women (ages 50-75 years) with incident malignant breast cancer compared to 613 matched controls with other types of cancer. Odds ratios were increased for the usual risk factors and after adjusting for these factors, increased risks were observed for exposures to PAHs (especially those derived from petroleum), solvents with active metabolites, inks, synthetic fibers and other textile fibers. Their findings were consistent with the hypothesis that breast tissue is more sensitive to adverse effects if exposure occurs when breast tissue is still proliferating[86].

In this study, increases in breast cancer were not observed in non-white CSE females or in females in the toner manufacturing group, the toner-exposed group that would have the higher exposure. In addition, after utilizing the Benjamin-Hochberg (B-H) approach to control the overall false-discovery rate (FDR), the increase seen in breast cancer in white female CSEs in this study was no longer statistically significant. One possible hypothesis for the increase in breast cancer observed in this study would be that it is a reflection of differences in the distribution of the known risk factors for breast cancer in the female CSE population versus the general US population; however, the data (e.g., reproductive history) are not available to substantiate this hypothesis. We will continue to monitor this finding in the next follow-up of the study.

Limitations of Study

The findings from this study need to be interpreted within the constraints of the study design and of the data available. The limitations of occupational mortality studies are well characterized and include: 1) mortality as a health outcome is an insensitive surrogate for diseases with low case-fatality rates (e.g., bladder cancer); 2) internal and external control populations may not match the exposed population on key characteristics; 3) lack of information on key potential confounding or modifying factors, such as cigarette smoking, reproductive and family history, 4) cause of death is subject to misclassification; however, this misclassification is likely to be non-differential relative to exposure; 5) inability to separate out effects of other exposures that may have occurred in the cohort; 6) underestimation of risks due to the healthy worker effect; 7) overestimation of risk because of chance findings due to multiple comparisons; 8) limited statistical power within particular subgroups (particularly for females and toner manufacturing population) and 9) possible incomplete ascertainment of deaths.

Despite these limitations, this study does provide a comprehensive picture of the causes of death including all occurrences of death from cancer and respiratory disease in Xerox workers exposed to conventional toner. It offers needed surveillance on the consequences of toner exposure.

CONCLUSION AND RECOMMENDATIONS

This study followed a large cohort of Xerox employees (33,671) over a period of up to 46 years to investigate potential adverse effects of toner exposure on all-cause and cause-specific mortality rates. The present analysis evaluated 5,424 mortality events occurring over 1,053,145 person-years of follow-up time (median follow-up time 33 years). The results of this analysis are consistent with the general mortality patterns typically found among healthy working populations.

We found no evidence that toner exposure increases the risk of all-cause mortality, or risk of cause-specific mortality for 23 categories of cause of death. In addition, for the five diseases (all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes) for which an increase in mortality might be hypothesized due to exposure to particulates, no increases were observed; in fact, statistically significant decreases in mortality in both white and non-white males were observed for these 5 causes of death compared to the general US population. Similarly, no significant increases were seen in exposed females for all cancers, lung cancer, respiratory disease, cardiovascular disease and diabetes.

APPENDIX A.

ICD9 and ICD10 codes used for categorization of outcomes

Outcome	ICD9 code	ICD10 code	Notes
Digestive Cancer	150-159	C15-C26	
Esophageal Cancer	150	C15	
Stomach Cancer	151	C16	
Colon Cancer	153	C18	
Cancer of the Rectum	154.1	C20	Does not include cancer of the rectosigmoid junction
Liver Cancer	155	C22	
Pancreatic Cancer	157	C25	
Lung Cancer	162	C34	
Skin Cancer	172	C43	Only includes melanoma
Breast Cancer	174	C50	
Prostate Cancer	185	C61	
Testicular Cancer	186	C62	
Bladder Cancer	188	C67	
Kidney Cancer	189	C64	
Brain Cancer	191	C71	
Leukemia	204-208	C91-C95	
Lymphomas and Multiple Myelomas	200-203	C81-C90, C96	
Diabetes	250	E10-E14	
Cardiovascular Disease	390-459	I00-I99	
Respiratory Disease	470-478, 490-519	J30-J98	
All Cancer	140-208	C00-C97	
All External Causes	E800-E999	V01-Y98	

APPENDIX B:

Table B1. Comparison of exposure groups (CSE, TME and overall) to the control group and pay method unknown group across pertinent characteristics.

	Exposed	CSE	TME	OKC	WEB	Controls	Unknown
Overall	21,509	20,614	900	150	751	10,556	467
Gender							
Male	19,916	19,165	756	122	635	8,339	330
Female	1,493	1,351	142	28	114	2,173	118
Unknown	100	98	2	.	2	44	19
Race							
Non-White	4,264	4,076	189	41	148	1,306	10
White	14,538	13,851	691	109	583	7,020	167
Unknown	2,707	2,687	20	.	20	2,230	290
Year of Birth							
1890	1	1	0	0	0	21	3
1900	8	8	0	0	0	135	11
1910	62	42	20	1	19	822	17
1920	434	381	53	6	47	1,532	60
1930	3,031	2,901	131	18	113	2,165	194
1940	11,458	11,107	352	43	309	3,865	182
1950	6,232	5,900	334	80	255	1,881	0
1960	283	274	10	2	8	135	0
	Median (IQR*)						
Age at entry into cohort (Years)	25(23,29)	25(23,28)	29(23,39)	26(23,33)	29(24,40)	27(22,38)	24(21,29)
NWF	26(23,31)	26(22,29)	35(26,44)	29(25,35)	39(26,45)	27(23,34)	22(22,33)
NWM	26(23,30)	26(23,29)	30(23,39)	26(23,33)	30(24,40)	26(22,33)	23(21,24)
WF	26(23,31)	26(23,30)	36(25,47)	31(25,37)	39(26,50)	35(25,44)	22(19,28)
WM	25(23,28)	25(23,28)	27(23,37)	26(23,31)	28(23,38)	26(21,36)	25(22,30)
Followup-Time (Years)							
NWF	27(25,30)	27(26,30)	24(18,31)	28(26,30)	20(18,32)	33(27,36)	41(41,43)
NWM	31(27,33)	31(27,33)	28(20,33)	28(27,29)	26(19,33)	33(26,37)	43(43,43)
WF	28(26,31)	28(27,31)	28(23,31)	27(27,28)	29(21,32)	33(28,37)	43(42,44)
WM	34(30,38)	34(30,39)	30(23,33)	28(27,30)	31(22,34)	35(28,40)	42(39,44)

*IQR = Interquartile Range, 25th and 75th percentiles

Table B2. The distribution of deaths in the study population across race, gender and exposure categories

	White Male	Non-White Male	White Female	Non-white Female	Total
Exposed	1898 (79.4)	406 (17.0)	69 (2.9)	18 (0.8)	2,391
CSE	1796 (79.8)	380 (16.9)	61 (2.7)	15 (0.7)	2,252
TME	102 (73.4)	26 (18.7)	8 (5.8)	3 (2.2)	139
OKC	15 (57.7)	8 (30.8)	0 (0.0)	3 (11.5)	26
Webster	87 (77.0)	18 (15.9)	8 (7.1)	0 (0.0)	113
Controls	2113 (73.4)	206 (7.2)	491 (17.1)	67 (2.3)	2,877
Censored	25 (83.3)	2 (6.7)	3 (10.0)	0 (0.0)	30
Unknown	108 (85.7)	1 (0.8)	16 (12.7)	1 (0.8)	126
Overall	4144 (76.4)	615 (11.3)	579 (10.7)	86 (1.6)	5,424

Table B3. The distribution of person years across the exposure categories by race and gender

	White Male	Non-White Male	White Female	Non-White Female
Exposed	539,451	118,751	32,881	8,659
-CSE	522,282	115,193	30,481	7,468
-TME	17,242	3,581	2,400	1,191
-OKC	2,503	766	439	327
-WEB	14,749	2,816	1,961	864
Control	241,672	24,940	54,541	13,396
Unknown	13,444	214	4,710	189
Overall	794,772	143,943	92,176	22,254

Table B4. Crude death rates across exposure groups among race and gender groups (per 1000 person years)

	White Male	Non-White Male	White Female	Non-White Female
Exposed	3.52	3.42	2.10	2.08
-CSE	3.44	3.30	2.00	2.01
-TME	5.92	7.26	3.33	2.52
-OKC	5.99	10.45	0.00	9.16
-WEB	5.90	6.39	4.08	0.00
Control	8.74	8.26	9.00	5.00
Unknown	8.03	4.68	3.40	5.29
Overall	5.21	4.27	6.28	3.86

Figure B1. Overall Survival Estimates (Control versus Exposed Employees) – all gender/race groups

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C1. SMR analysis results for eligible white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	54	50.46	794493.83	1.07	(0.8,1.4)
Cancer of the stomach	44	38.16	794493.83	1.15	(0.84,1.55)
Cancer of the colon	112	114.07	794493.83	0.98	(0.81,1.18)
Cancer of the rectum	26	19.8	794493.83	1.31	(0.86,1.92)
Cancer of the liver	24	38.07	794493.83	0.63	(0.4,0.94)
Cancer of the pancreas	78	77.39	794493.83	1.01	(0.8,1.26)
Cancer of the lung	416	512.45	794493.83	0.81	(0.74,0.89)
Cancer of the skin	44	36.98	794493.83	1.19	(0.86,1.6)
Cancer of the breast	0	0.96	794493.83	.	
Cancer of the bladder	37	32.52	794493.83	1.14	(0.8,1.57)
Cancer of the testis	3	4.9	794493.83		
Cancer of the prostate	82	80.83	794493.83	1.01	(0.81,1.26)
Cancer of the kidney	31	43.61	794493.83	0.71	(0.48,1.01)
Cancer of the brain	46	51.1	794493.83	0.9	(0.66,1.2)
Leukemia	56	58.29	794493.83	0.96	(0.73,1.25)
Lymphomas and multiple myelomas	72	97.01	794493.83	0.74	(0.58,0.93)
Diabetes	75	131.78	794493.83	0.57	(0.45,0.71)
Cardiovascular disease	1428	1957.18	794493.83	0.73	(0.69,0.77)
Respiratory disease	180	270.19	794493.83	0.67	(0.57,0.77)
All external	415	665.94	794493.83	0.62	(0.56,0.69)
All cancer	1296	1473.06	794493.83	0.88	(0.83,0.93)
All causes	4144	5527.69	794493.83	0.75	(0.73,0.77)
Cancer of the digestive system	358	358.88	794493.83	1	(0.9,1.11)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C2: SMR analysis results for exposed white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	27	29.4	539148.6	0.92	(0.61,1.34)
Cancer of the stomach	16	20.07	539148.6	0.8	(0.46,1.29)
Cancer of the colon	54	58.83	539148.6	0.92	(0.69,1.2)
Cancer of the rectum	9	10.66	539148.6	0.84	(0.39,1.6)
Cancer of the liver	14	22.6	539148.6	0.62	(0.34,1.04)
Cancer of the pancreas	45	42.78	539148.6	1.05	(0.77,1.41)
Cancer of the lung	178	273.22	539148.6	0.65	(0.56,0.75)
Cancer of the skin	27	23.06	539148.6	1.17	(0.77,1.7)
Cancer of the breast	0	0.56	539148.6	.	
Cancer of the bladder	14	15.56	539148.6	0.9	(0.49,1.51)
Cancer of the testis	0	3.33	539148.6	.	
Cancer of the prostate	27	30.88	539148.6	0.87	(0.58,1.27)
Cancer of the kidney	18	25.05	539148.6	0.72	(0.43,1.14)
Cancer of the brain	26	31.66	539148.6	0.82	(0.54,1.2)
Leukemia	26	32.04	539148.6	0.81	(0.53,1.19)
Lymphomas and multiple myelomas	37	54.65	539148.6	0.68	(0.48,0.93)
Diabetes	38	74.53	539148.6	0.51	(0.36,0.7)
Cardiovascular disease	586	947.83	539148.6	0.62	(0.57,0.67)
Respiratory disease	63	124.73	539148.6	0.51	(0.39,0.65)
All external	246	445.66	539148.6	0.55	(0.49,0.63)
All cancer	604	795.22	539148.6	0.76	(0.7,0.82)
All causes	1898	2968.95	539148.6	0.64	(0.61,0.67)
Cancer of the digestive system	174	195.5	539148.6	0.89	(0.76,1.03)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C3: SMR analysis results for control white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	25	19.87	241671.92	1.26	(0.81,1.86)
Cancer of the stomach	28	17.14	241671.92	1.63	(1.09,2.36)
Cancer of the colon	54	52.34	241671.92	1.03	(0.78,1.35)
Cancer of the rectum	16	8.65	241671.92	1.85	(1.06,3)
Cancer of the liver	9	14.63	241671.92	0.62	(0.28,1.17)
Cancer of the pancreas	28	32.71	241671.92	0.86	(0.57,1.24)
Cancer of the lung	221	225.89	241671.92	0.98	(0.85,1.12)
Cancer of the skin	16	13.14	241671.92	1.22	(0.7,1.98)
Cancer of the breast	0	0.37	241671.92	.	
Cancer of the bladder	23	16.1	241671.92	1.43	(0.91,2.14)
Cancer of the testis	2	1.48	241671.92		
Cancer of the prostate	48	47.67	241671.92	1.01	(0.74,1.33)
Cancer of the kidney	13	17.53	241671.92	0.74	(0.39,1.27)
Cancer of the brain	19	18.35	241671.92	1.04	(0.62,1.62)
Leukemia	29	24.84	241671.92	1.17	(0.78,1.68)
Lymphomas and multiple myelomas	35	40.04	241671.92	0.87	(0.61,1.22)
Diabetes	37	54.14	241671.92	0.68	(0.48,0.94)
Cardiovascular disease	796	959.19	241671.92	0.83	(0.77,0.89)
Respiratory disease	109	138.19	241671.92	0.79	(0.65,0.95)
All external	160	209.32	241671.92	0.76	(0.65,0.89)
All cancer	647	641.16	241671.92	1.01	(0.93,1.09)
All causes	2113	2428.23	241671.92	0.87	(0.83,0.91)
Cancer of the digestive system	169	154.6	241671.92	1.09	(0.93,1.27)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C4: SMR analysis results for CSE white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	25	28.29	522014.81	0.88	(0.57,1.3)
Cancer of the stomach	14	19.25	522014.81	0.73	(0.4,1.22)
Cancer of the colon	51	56.36	522014.81	0.9	(0.67,1.19)
Cancer of the rectum	9	10.24	522014.81	0.88	(0.4,1.67)
Cancer of the liver	13	21.73	522014.81	0.6	(0.32,1.02)
Cancer of the pancreas	41	41.11	522014.81	1	(0.72,1.35)
Cancer of the lung	165	262.16	522014.81	0.63	(0.54,0.73)
Cancer of the skin	27	22.26	522014.81	1.21	(0.8,1.76)
Cancer of the breast	0	0.54	522014.81	.	
Cancer of the bladder	13	14.84	522014.81	0.88	(0.47,1.5)
Cancer of the testis	0	3.24	522014.81	.	
Cancer of the prostate	25	29.05	522014.81	0.86	(0.56,1.27)
Cancer of the kidney	17	24.11	522014.81	0.7	(0.41,1.13)
Cancer of the brain	25	30.56	522014.81	0.82	(0.53,1.21)
Leukemia	26	30.78	522014.81	0.84	(0.55,1.24)
Lymphomas and multiple myelomas	35	52.55	522014.81	0.67	(0.46,0.93)
Diabetes	36	71.63	522014.81	0.5	(0.35,0.7)
Cardiovascular disease	550	906.57	522014.81	0.61	(0.56,0.66)
Respiratory disease	58	118.67	522014.81	0.49	(0.37,0.63)
All external	237	430.77	522014.81	0.55	(0.48,0.62)
All cancer	569	763.26	522014.81	0.75	(0.69,0.81)
All causes	1796	2849.59	522014.81	0.63	(0.6,0.66)
Cancer of the digestive system	161	187.7	522014.81	0.86	(0.73,1)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C5: SMR analysis results for TME white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	2	1.11	17231.31		
Cancer of the stomach	2	0.82	17231.31		
Cancer of the colon	3	2.47	17231.31		
Cancer of the rectum	0	0.42	17231.31	.	
Cancer of the liver	1	0.87	17231.31		
Cancer of the pancreas	4	1.68	17231.31		
Cancer of the lung	13	11.07	17231.31	1.17	(0.63,2.01)
Cancer of the skin	0	0.8	17231.31	.	
Cancer of the breast	0	0.02	17231.31	.	
Cancer of the bladder	1	0.72	17231.31		
Cancer of the testis	0	0.09	17231.31	.	
Cancer of the prostate	2	1.83	17231.31		
Cancer of the kidney	1	0.94	17231.31		
Cancer of the brain	1	1.11	17231.31		
Leukemia	0	1.26	17231.31	.	
Lymphomas and multiple myelomas	2	2.1	17231.31		
Diabetes	2	2.91	17231.31		
Cardiovascular disease	36	41.32	17231.31	0.87	(0.61,1.21)
Respiratory disease	5	6.07	17231.31		
All external	9	14.98	17231.31	0.6	(0.27,1.14)
All cancer	35	32.01	17231.31	1.09	(0.76,1.52)
All causes	102	119.66	17231.31	0.85	(0.7,1.03)
Cancer of the digestive system	13	7.82	17231.31	1.66	(0.89,2.84)

Table C6

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Table C7

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APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C8: SMR analysis results for eligible non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	4	12.92	143931.71		
Cancer of the stomach	7	10.88	143931.71	0.64	(0.26,1.33)
Cancer of the colon	15	19.31	143931.71	0.78	(0.43,1.28)
Cancer of the rectum	0	3.21	143931.71	.	
Cancer of the liver	6	13.54	143931.71	0.44	(0.16,0.96)
Cancer of the pancreas	10	12.96	143931.71	0.77	(0.37,1.42)
Cancer of the lung	45	86.69	143931.71	0.52	(0.38,0.69)
Cancer of the skin	0	0.48	143931.71	.	
Cancer of the breast	0	0.21	143931.71	.	
Cancer of the bladder	1	2.62	143931.71		
Cancer of the testis	1	0.26	143931.71		
Cancer of the prostate	14	16.96	143931.71	0.83	(0.45,1.38)
Cancer of the kidney	5	5.57	143931.71		
Cancer of the brain	5	3.93	143931.71		
Leukemia	5	7.41	143931.71		
Lymphomas and multiple myelomas	12	14.4	143931.71	0.83	(0.43,1.46)
Diabetes	20	35.64	143931.71	0.56	(0.34,0.87)
Cardiovascular disease	206	374.99	143931.71	0.55	(0.48,0.63)
Respiratory disease	17	33.55	143931.71	0.51	(0.3,0.81)
All external	75	187.54	143931.71	0.4	(0.31,0.5)
All cancer	151	258.38	143931.71	0.58	(0.49,0.69)
All causes	615	1230.4	143931.71	0.5	(0.46,0.54)
Cancer of the digestive system	44	76.13	143931.71	0.58	(0.42,0.78)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C9: SMR analysis results for exposed non- white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	3	9.58	118735.88		
Cancer of the stomach	5	8	118735.88		
Cancer of the colon	12	14.37	118735.88	0.83	(0.43,1.46)
Cancer of the rectum	0	2.43	118735.88	.	
Cancer of the liver	6	10.79	118735.88	0.56	(0.2,1.21)
Cancer of the pancreas	7	9.73	118735.88	0.72	(0.29,1.48)
Cancer of the lung	29	63.89	118735.88	0.45	(0.3,0.65)
Cancer of the skin	0	0.37	118735.88	.	
Cancer of the breast	0	0.17	118735.88	.	
Cancer of the bladder	0	1.83	118735.88	.	
Cancer of the testis	1	0.22	118735.88		
Cancer of the prostate	10	10.62	118735.88	0.94	(0.45,1.73)
Cancer of the kidney	3	4.28	118735.88		
Cancer of the brain	5	3.11	118735.88		
Leukemia	4	5.66	118735.88		
Lymphomas and multiple myelomas	7	11.05	118735.88	0.63	(0.25,1.3)
Diabetes	13	27.36	118735.88	0.48	(0.25,0.81)
Cardiovascular disease	124	276.97	118735.88	0.45	(0.37,0.53)
Respiratory disease	9	24.26	118735.88	0.37	(0.17,0.7)
All external	49	154.91	118735.88	0.32	(0.23,0.42)
All cancer	106	191.94	118735.88	0.55	(0.45,0.67)
All causes	406	942.53	118735.88	0.43	(0.39,0.47)
Cancer of the digestive system	33	57.4	118735.88	0.57	(0.4,0.81)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C10: SMR analysis results for control non- white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	3.31	24939.89		
Cancer of the stomach	2	2.86	24939.89		
Cancer of the colon	3	4.9	24939.89		
Cancer of the rectum	0	0.77	24939.89	.	
Cancer of the liver	0	2.73	24939.89	.	
Cancer of the pancreas	3	3.21	24939.89		
Cancer of the lung	16	22.62	24939.89	0.71	(0.4,1.15)
Cancer of the skin	0	0.11	24939.89	.	
Cancer of the breast	0	0.04	24939.89	.	
Cancer of the bladder	1	0.79	24939.89		
Cancer of the testis	0	0.04	24939.89	.	
Cancer of the prostate	4	6.31	24939.89		
Cancer of the kidney	2	1.28	24939.89		
Cancer of the brain	0	0.82	24939.89	.	
Leukemia	1	1.74	24939.89		
Lymphomas and multiple myelomas	5	3.32	24939.89		
Diabetes	7	8.21	24939.89	0.85	(0.34,1.76)
Cardiovascular disease	80	97.31	24939.89	0.82	(0.65,1.02)
Respiratory disease	8	9.23	24939.89	0.87	(0.37,1.71)
All external	25	32.32	24939.89	0.77	(0.5,1.14)
All cancer	45	65.94	24939.89	0.68	(0.5,0.91)
All causes	206	285.53	24939.89	0.72	(0.63,0.83)
Cancer of the digestive system	11	18.58	24939.89	0.59	(0.3,1.06)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C11: SMR analysis results for CSE non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	2	9.25	115182.56		
Cancer of the stomach	5	7.74	115182.56		
Cancer of the colon	10	13.89	115182.56	0.72	(0.35,1.32)
Cancer of the rectum	0	2.35	115182.56	.	
Cancer of the liver	6	10.43	115182.56	0.58	(0.21,1.25)
Cancer of the pancreas	7	9.4	115182.56	0.74	(0.3,1.53)
Cancer of the lung	28	61.72	115182.56	0.45	(0.3,0.66)
Cancer of the skin	0	0.35	115182.56	.	
Cancer of the breast	0	0.16	115182.56	.	
Cancer of the bladder	0	1.77	115182.56	.	
Cancer of the testis	1	0.21	115182.56		
Cancer of the prostate	8	10.27	115182.56	0.78	(0.34,1.53)
Cancer of the kidney	3	4.14	115182.56		
Cancer of the brain	5	3.01	115182.56		
Leukemia	3	5.47	115182.56		
Lymphomas and multiple myelomas	7	10.69	115182.56	0.65	(0.26,1.35)
Diabetes	12	26.46	115182.56	0.45	(0.23,0.79)
Cardiovascular disease	116	267.86	115182.56	0.43	(0.36,0.52)
Respiratory disease	8	23.47	115182.56	0.34	(0.15,0.67)
All external	48	150.4	115182.56	0.32	(0.24,0.42)
All cancer	96	185.51	115182.56	0.52	(0.42,0.63)
All causes	380	912.53	115182.56	0.42	(0.38,0.46)
Cancer of the digestive system	30	55.48	115182.56	0.54	(0.36,0.77)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C12: SMR analysis results for TME non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	0.33	3577.07		
Cancer of the stomach	0	0.27	3577.07	.	
Cancer of the colon	2	0.49	3577.07		
Cancer of the rectum	0	0.08	3577.07	.	
Cancer of the liver	0	0.36	3577.07	.	
Cancer of the pancreas	0	0.33	3577.07	.	
Cancer of the lung	1	2.21	3577.07		
Cancer of the skin	0	0.01	3577.07	.	
Cancer of the breast	0	0.01	3577.07	.	
Cancer of the bladder	0	0.06	3577.07	.	
Cancer of the testis	0	0.01	3577.07	.	
Cancer of the prostate	2	0.36	3577.07		
Cancer of the kidney	0	0.14	3577.07	.	
Cancer of the brain	0	0.1	3577.07	.	
Leukemia	1	0.18	3577.07		
Lymphomas and multiple myelomas	0	0.37	3577.07	.	
Diabetes	1	0.91	3577.07		
Cardiovascular disease	8	9.24	3577.07	0.87	(0.37,1.71)
Respiratory disease	1	0.8	3577.07		
All external	1	4.54	3577.07		
All cancer	10	6.53	3577.07	1.53	(0.73,2.82)
All causes	26	30.36	3577.07	0.86	(0.56,1.25)
Cancer of the digestive system	3	1.95	3577.07		

Table C13

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Table C14

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APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C15: SMR analysis results for eligible white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	3	1.84	92176.32		
Cancer of the stomach	4	3.39	92176.32		
Cancer of the colon	12	16.52	92176.32	0.73	(0.38,1.27)
Cancer of the rectum	1	2.08	92176.32		
Cancer of the liver	3	2.86	92176.32		
Cancer of the pancreas	8	9.92	92176.32	0.81	(0.35,1.59)
Cancer of the lung	74	47.95	92176.32	1.54	(1.21,1.94)
Cancer of the skin	1	2.69	92176.32		
Cancer of the breast	45	38.35	92176.32	1.17	(0.86,1.57)
Cancer of the bladder	4	2.15	92176.32		
Cancer of the testis	0	0	92176.32	.	
Cancer of the prostate	0	0	92176.32	.	
Cancer of the kidney	0	3.36	92176.32	.	
Cancer of the brain	1	4.99	92176.32		
Leukemia	4	6.33	92176.32		
Lymphomas and multiple myelomas	12	11.3	92176.32	1.06	(0.55,1.86)
Diabetes	10	18.91	92176.32	0.53	(0.25,0.97)
Cardiovascular disease	180	236.59	92176.32	0.76	(0.65,0.88)
Respiratory disease	35	41.78	92176.32	0.84	(0.58,1.17)
All external	33	29.91	92176.32	1.1	(0.76,1.55)
All cancer	210	199.72	92176.32	1.05	(0.91,1.2)
All causes	579	655	92176.32	0.88	(0.81,0.96)
Cancer of the digestive system	31	40.19	92176.32	0.77	(0.52,1.09)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C16: SMR analysis results for exposed white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.24	32881.17	.	
Cancer of the stomach	0	0.47	32881.17	.	
Cancer of the colon	1	2.05	32881.17		
Cancer of the rectum	0	0.3	32881.17	.	
Cancer of the liver	0	0.45	32881.17	.	
Cancer of the pancreas	0	1.31	32881.17	.	
Cancer of the lung	5	7.4	32881.17		
Cancer of the skin	1	0.66	32881.17		
Cancer of the breast	14	7.53	32881.17	1.86	(1.02,3.12)
Cancer of the bladder	0	0.23	32881.17	.	
Cancer of the testis	0	0	32881.17	.	
Cancer of the prostate	0	0	32881.17	.	
Cancer of the kidney	0	0.51	32881.17	.	
Cancer of the brain	0	1.07	32881.17	.	
Leukemia	0	1.05	32881.17	.	
Lymphomas and multiple myelomas	1	1.6	32881.17		
Diabetes	0	2.63	32881.17	.	
Cardiovascular disease	6	21.46	32881.17	0.28	(0.1,0.61)
Respiratory disease	3	4.65	32881.17		
All external	11	9.46	32881.17	1.16	(0.58,2.08)
All cancer	33	32.45	32881.17	1.02	(0.7,1.43)
All causes	69	88.03	32881.17	0.78	(0.61,0.99)
Cancer of the digestive system	1	5.29	32881.17		

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C17: SMR analysis results for control white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	3	1.51	54540.59		
Cancer of the stomach	4	2.75	54540.59		
Cancer of the colon	11	13.67	54540.59	0.8	(0.4,1.44)
Cancer of the rectum	1	1.68	54540.59		
Cancer of the liver	3	2.27	54540.59		
Cancer of the pancreas	8	8.13	54540.59	0.98	(0.42,1.94)
Cancer of the lung	67	38.32	54540.59	1.75	(1.36,2.22)
Cancer of the skin	0	1.9	54540.59	.	
Cancer of the breast	27	28.97	54540.59	0.93	(0.61,1.36)
Cancer of the bladder	4	1.81	54540.59		
Cancer of the testis	0	0	54540.59	.	
Cancer of the prostate	0	0	54540.59	.	
Cancer of the kidney	0	2.69	54540.59	.	
Cancer of the brain	1	3.69	54540.59		
Leukemia	4	4.97	54540.59		
Lymphomas and multiple myelomas	9	9.17	54540.59	0.98	(0.45,1.86)
Diabetes	10	15.35	54540.59	0.65	(0.31,1.2)
Cardiovascular disease	167	202.17	54540.59	0.83	(0.71,0.96)
Respiratory disease	31	35.28	54540.59	0.88	(0.6,1.25)
All external	21	19.01	54540.59	1.1	(0.68,1.69)
All cancer	169	157.73	54540.59	1.07	(0.92,1.25)
All causes	491	533.85	54540.59	0.92	(0.84,1)
Cancer of the digestive system	30	32.96	54540.59	0.91	(0.61,1.3)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C18: SMR analysis results for CSE white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.18	30481.4	.	
Cancer of the stomach	0	0.37	30481.4	.	
Cancer of the colon	1	1.59	30481.4		
Cancer of the rectum	0	0.24	30481.4	.	
Cancer of the liver	0	0.36	30481.4	.	
Cancer of the pancreas	0	1.03	30481.4	.	
Cancer of the lung	3	5.95	30481.4		
Cancer of the skin	1	0.58	30481.4		
Cancer of the breast	14	6.47	30481.4	2.17	(1.18,3.63)
Cancer of the bladder	0	0.17	30481.4	.	
Cancer of the testis	0	0	30481.4	.	
Cancer of the prostate	0	0	30481.4	.	
Cancer of the kidney	0	0.41	30481.4	.	
Cancer of the brain	0	0.93	30481.4	.	
Leukemia	0	0.87	30481.4	.	
Lymphomas and multiple myelomas	1	1.28	30481.4		
Diabetes	0	2.09	30481.4	.	
Cardiovascular disease	4	15.16	30481.4		
Respiratory disease	2	3.41	30481.4		
All external	11	8.66	30481.4	1.27	(0.63,2.27)
All cancer	30	26.75	30481.4	1.12	(0.76,1.6)
All causes	61	69.98	30481.4	0.87	(0.67,1.12)
Cancer of the digestive system	1	4.17	30481.4		

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C19: SMR analysis results for TME white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.05	2399.77	.	
Cancer of the stomach	0	0.09	2399.77	.	
Cancer of the colon	0	0.45	2399.77	.	
Cancer of the rectum	0	0.06	2399.77	.	
Cancer of the liver	0	0.08	2399.77	.	
Cancer of the pancreas	0	0.29	2399.77	.	
Cancer of the lung	2	1.45	2399.77		
Cancer of the skin	0	0.07	2399.77	.	
Cancer of the breast	0	1.06	2399.77	.	
Cancer of the bladder	0	0.06	2399.77	.	
Cancer of the testis	0	0	2399.77	.	
Cancer of the prostate	0	0	2399.77	.	
Cancer of the kidney	0	0.1	2399.77	.	
Cancer of the brain	0	0.14	2399.77	.	
Leukemia	0	0.18	2399.77	.	
Lymphomas and multiple myelomas	0	0.32	2399.77	.	
Diabetes	0	0.54	2399.77	.	
Cardiovascular disease	2	6.3	2399.77		
Respiratory disease	1	1.25	2399.77		
All external	0	0.8	2399.77	.	
All cancer	3	5.7	2399.77		
All causes	8	18.05	2399.77	0.44	(0.19,0.87)
Cancer of the digestive system	0	1.13	2399.77	.	

Table C20

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Table C21

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APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C22: SMR analysis results for eligible non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.62	22254.04	.	
Cancer of the stomach	1	0.97	22254.04		
Cancer of the colon	3	2.75	22254.04		
Cancer of the rectum	0	0.31	22254.04	.	
Cancer of the liver	1	0.71	22254.04		
Cancer of the pancreas	1	1.66	22254.04		
Cancer of the lung	6	6.47	22254.04	0.93	(0.34,2.02)
Cancer of the skin	0	0.07	22254.04	.	
Cancer of the breast	6	7.49	22254.04	0.8	(0.29,1.74)
Cancer of the bladder	0	0.27	22254.04	.	
Cancer of the testis	0	0	22254.04	.	
Cancer of the prostate	0	0	22254.04	.	
Cancer of the kidney	1	0.43	22254.04		
Cancer of the brain	2	0.42	22254.04		
Leukemia	1	0.86	22254.04		
Lymphomas and multiple myelomas	0	1.62	22254.04	.	
Diabetes	5	5.68	22254.04		
Cardiovascular disease	25	40.08	22254.04	0.62	(0.4,0.92)
Respiratory disease	5	3.87	22254.04		
All external	8	7.6	22254.04	1.05	(0.45,2.07)
All cancer	29	33.06	22254.04	0.88	(0.59,1.26)
All causes	86	119.22	22254.04	0.72	(0.58,0.89)
Cancer of the digestive system	6	7.54	22254.04	0.8	(0.29,1.73)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C23: SMR analysis results for exposed non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.13	8659.31	.	
Cancer of the stomach	0	0.23	8659.31	.	
Cancer of the colon	0	0.65	8659.31	.	
Cancer of the rectum	0	0.08	8659.31	.	
Cancer of the liver	0	0.18	8659.31	.	
Cancer of the pancreas	0	0.36	8659.31	.	
Cancer of the lung	3	1.54	8659.31		
Cancer of the skin	0	0.02	8659.31	.	
Cancer of the breast	2	2.28	8659.31		
Cancer of the bladder	0	0.05	8659.31	.	
Cancer of the testis	0	0	8659.31	.	
Cancer of the prostate	0	0	8659.31	.	
Cancer of the kidney	1	0.11	8659.31		
Cancer of the brain	0	0.12	8659.31	.	
Leukemia	1	0.24	8659.31		
Lymphomas and multiple myelomas	0	0.4	8659.31	.	
Diabetes	0	1.27	8659.31	.	
Cardiovascular disease	1	8.64	8659.31		
Respiratory disease	2	0.97	8659.31		
All external	3	3.03	8659.31		
All cancer	8	8.52	8659.31	0.94	(0.41,1.85)
All causes	18	30.66	8659.31	0.59	(0.35,0.93)
Cancer of the digestive system	0	1.76	8659.31	.	

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C24: SMR analysis results for control non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.48	13396.25	.	
Cancer of the stomach	1	0.72	13396.25		
Cancer of the colon	3	2.06	13396.25		
Cancer of the rectum	0	0.23	13396.25	.	
Cancer of the liver	1	0.51	13396.25		
Cancer of the pancreas	1	1.27	13396.25		
Cancer of the lung	3	4.85	13396.25		
Cancer of the skin	0	0.05	13396.25	.	
Cancer of the breast	4	5.12	13396.25		
Cancer of the bladder	0	0.22	13396.25	.	
Cancer of the testis	0	0	13396.25	.	
Cancer of the prostate	0	0	13396.25	.	
Cancer of the kidney	0	0.32	13396.25	.	
Cancer of the brain	2	0.29	13396.25		
Leukemia	0	0.62	13396.25	.	
Lymphomas and multiple myelomas	0	1.19	13396.25	.	
Diabetes	5	4.32	13396.25		
Cardiovascular disease	23	30.8	13396.25	0.75	(0.47,1.12)
Respiratory disease	3	2.86	13396.25		
All external	5	4.5	13396.25		
All cancer	21	24.11	13396.25	0.87	(0.54,1.33)
All causes	67	86.93	13396.25	0.77	(0.6,0.98)
Cancer of the digestive system	6	5.67	13396.25	1.06	(0.39,2.3)

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C25: SMR analysis results for CSE non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.09	7467.92	.	
Cancer of the stomach	0	0.18	7467.92	.	
Cancer of the colon	0	0.48	7467.92	.	
Cancer of the rectum	0	0.06	7467.92	.	
Cancer of the liver	0	0.14	7467.92	.	
Cancer of the pancreas	0	0.25	7467.92	.	
Cancer of the lung	3	1.11	7467.92		
Cancer of the skin	0	0.01	7467.92	.	
Cancer of the breast	2	1.82	7467.92		
Cancer of the bladder	0	0.03	7467.92	.	
Cancer of the testis	0	0	7467.92	.	
Cancer of the prostate	0	0	7467.92	.	
Cancer of the kidney	1	0.08	7467.92		
Cancer of the brain	0	0.1	7467.92	.	
Leukemia	0	0.19	7467.92	.	
Lymphomas and multiple myelomas	0	0.3	7467.92	.	
Diabetes	0	0.91	7467.92	.	
Cardiovascular disease	1	6.34	7467.92		
Respiratory disease	1	0.73	7467.92		
All external	3	2.63	7467.92		
All cancer	7	6.45	7467.92	1.08	(0.44,2.23)
All causes	15	23.72	7467.92	0.63	(0.35,1.04)
Cancer of the digestive system	0	1.29	7467.92	.	

APPENDIX C: Tables of SMRs for each cause of death for each race and gender group

Table C26: SMR analysis results for TME non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.04	1191.39	.	
Cancer of the stomach	0	0.06	1191.39	.	
Cancer of the colon	0	0.17	1191.39	.	
Cancer of the rectum	0	0.02	1191.39	.	
Cancer of the liver	0	0.05	1191.39	.	
Cancer of the pancreas	0	0.11	1191.39	.	
Cancer of the lung	0	0.43	1191.39	.	
Cancer of the skin	0	0	1191.39	.	
Cancer of the breast	0	0.47	1191.39	.	
Cancer of the bladder	0	0.02	1191.39	.	
Cancer of the testis	0	0	1191.39	.	
Cancer of the prostate	0	0	1191.39	.	
Cancer of the kidney	0	0.03	1191.39	.	
Cancer of the brain	0	0.03	1191.39	.	
Leukemia	1	0.05	1191.39		
Lymphomas and multiple myelomas	0	0.1	1191.39	.	
Diabetes	0	0.36	1191.39	.	
Cardiovascular disease	0	2.3	1191.39	.	
Respiratory disease	1	0.24	1191.39		
All external	0	0.4	1191.39	.	
All cancer	1	2.07	1191.39		
All causes	3	6.95	1191.39		
Cancer of the digestive system	0	0.47	1191.39	.	

Table C27

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Table C28

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SANITIZED VERSION

Table D1

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REVISED REPORT

A 40-Year Retrospective Cohort Study of Toner-exposed Employees of the Xerox Corporation

Alison Abraham, PhD, MS, MHS

Stephen Gange, PhD

Gayle Springer, MLA

Jonathan Samet, MD, MS

Susan B Rawleigh, MS, MPH

Larry R. Glass, PhD, MPH

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The Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe Street, Baltimore, MD 21205

Note: There was an error in the initial SMR analysis that was discovered while doing the subsequent analysis that tracked vital status through the end of 2006. Some selected deaths were double counted as both exposed and control deaths. This occurred in instances in which an employee incurred time in the control group followed by time in the exposed group and the deaths were counted under both groups. As per the protocol, once an employee became toner-exposed (even for one day), he/she could not accumulate any more control time. Therefore, they should have only been counted under the toner-exposed group. This report corrects these errors. All the changes were in the SMRs from the control group. The differences were fairly minor. The largest differences were in testicular cancer in white male controls (SMR 2.21 dropped to 1.48); esophageal cancer in non-white males (SMR dropped from 0.83 to 0.41); and lymphomas and multiple myelomas (SMR 1.36 dropped to 1.19). The remainder of the differences were 0.09 or less. A table detailing the differences is included as Appendix C, Table 1.

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SUMMARY

This report provides the findings of an epidemiological analysis of mortality among Xerox employees. The work was carried out by researchers in the Department of Epidemiology of the Johns Hopkins Bloomberg School of Public Health, using data gathered by Xerox. The overall goal was to assess if occupational exposure to toner, either in manufacturing of the toner itself, or in the servicing of copying equipment, had any adverse effect on employee mortality. The study was carried out as part of a longstanding and ongoing effort by Xerox to monitor the health of its employees. Toner is a particulate material containing particles of a size that can be inhaled into the lung. Because recent studies in the scientific literature have shown an increase in the risk of premature mortality and cancer associated with long-term exposure to particulate air pollution in the general population, Xerox has also sought to ensure that similar effects were not being experienced by its toner-exposed workers.

The study design used is called a "retrospective cohort study". In this design the workers are tracked over time to capture any deaths and their causes; it is termed "retrospective" because all events are in the past, and the data are gathered using a variety of record systems that have collected and retained the needed information. To determine if toner exposure does increase the risk for mortality for specific causes of death, comparison was made between the mortality rates in the toner exposed workers and rates in control workers, not exposed to toner and to the US population in general. A ratio of the age-adjusted rates, called the standardized mortality ratio, or SMR, was used for this comparison.

The study group, called the cohort, was assembled from work records and included 33,671 workers, employed between 1960 and 1982, that met the eligibility criteria for the study. For all of their work experience through 1998, they were classified as exposed or not exposed to toner, based on their work histories; once workers were classified as exposed, they remained in this category, even if they returned to a job not involving toner exposure. The vital status (i.e. dead or alive designation) of each worker was determined through the use of various national databases. Information on the cause of death was obtained and coded using a widely utilized and standard classification scheme. Vital status was tracked through the end of 1999.

Overall, the study did not show that Xerox workers were at greater risk of dying than people in the US population in general. In fact, the SMRs for Xerox workers were below one, indicating that they were less likely to die than the population in general. This finding was similar for both the toner-exposed workers and for the control group. Most likely, the SMRS are less than one because Xerox employees, like other employed people tend to be healthier than the general population due to the fact that the severely ill and disabled are typically excluded from the workforce. This is known as "the healthy worker effect." The findings of the study also suggested that toner exposure was not associated with any increase in risk for any particular cancer or disease.

As with any study or study design, this study has some limitations. When mortality is used as the health indicator, more subtle adverse effects of toner exposure that do not lead to death could possibly be missed. Also, this study could not account for the effects of some potentially important factors, such as smoking, because such information was not available. There is also the possibility that the comparison control groups, both the unexposed Xerox workers and the general US population,

were not sufficiently similar to the toner-exposed workers to draw comparisons. These inherent limitations are common to most occupational health studies of the retrospective cohort design.

In spite of these limitations, the study provides useful information on patterns of death among Xerox workers, particularly those who have been occupationally exposed to toner. The results of this analysis are consistent with the general mortality patterns among healthy working populations. There was no evidence that occupational exposure to toner increased the risk of all-cause or cause-specific mortality. However, ongoing follow-up of the cohort should be maintained, with a repeated assessment of mortality patterns as this population continues to age.

INTRODUCTION

Adverse health effects due to acute and chronic inhalation of fine particles have been the subject of epidemiologic research in a variety of contexts. The general population is continually exposed to airborne particles, from natural and man-made sources that are ubiquitous indoors and outdoors. An association between mortality and chronic exposure to ambient particulate pollution has been found in a number of studies [1,2,3] and this finding has been part of the rationale for a strengthening of standards for airborne particulate matter in the United States and elsewhere. Certain occupational groups have even higher exposures to particulate matter than the general public, and the adverse health effects due to inhalation of some agents are well documented, such as the pneumoconioses and the lung cancer risk associated with asbestos. Given findings of increased risk for lung cancer associated with outdoor air pollution and with specific occupational agents as noted above, increased cancer risk poses a potential concern among occupational groups exposed to workplace airborne particles. Studies in the general population also link particulate matter to cardiovascular disease mortality [4].

As part of its longstanding and ongoing commitment to workplace health and safety, the Xerox Corporation has conducted multi-decade studies of its workers with occupational exposures to toners. Toners are fine powders composed mainly of plastics and colorants and minor quantities of functional additives. Historically, the median particle size ranged from 8 to 10 micrometers. However, in recent years, advances in technology have led to smaller particle sizes being used. Previously, these particles may have contained contaminants such as polycyclic aromatic hydrocarbons (PAH) and nitropyrenes as a result of the manufacturing process. In 1980, Xerox introduced a standard to control the level of PAH (PAH levels – total specified < 1ppm; non-specified < 10 ppm) and nitropyrenes (< 1.2 ppm) in the carbon black that they used. In 1990, Xerox further reduced the level for nitropyrenes to < 0.15 ppm. Therefore, since 1990, levels of such contaminants have become negligible. Further, the mean total dust levels have declined substantially in Xerox's toner manufacturing facilities with mean dust levels ranging from 6.2-9.6 mg/m^3 in the 1960's to 0.8-7.6 mg/m^3 in the 1970's to 0.9-1.3 mg/m^3 in the 1980's. In 1988, Xerox adopted a "Xerox Exposure Limit" for total dust of 2.5 mg/m^3. The current mean total dust level in the toner manufacturing facilities is less than 1 mg/m^3. These levels are much lower then the current exposure limit of 15 mg/m^3 for total dust set by the US government (OSHA). Exposures for CSEs to airborne toner are typically five to ten times lower than in the manufacturing plants. Xerox initiated this mortality study, along with a concurrent morbidity study, in order to identify if there were any potential adverse health effects among its workers that might be associated with the occupational inhalation of toner particles.

Animal models have been used to explore the potential oncogenicity of inhaled toner. Studies in rats provide no indication of an increased risk of lung tumors in rats exposed to high levels of toner, though there was evidence of particulate matter retention, inflammatory response and pulmonary fibrosis [5,6,7,8]. There is a similar dearth of epidemiologic evidence for a higher risk of morbidity or mortality in human populations. Occupational studies of carbon black, a colorant in black toner, have found mixed evidence for a lung cancer excess among exposed workers, but no suggestion of any trend of an increase in risk with accumulated exposure [9,10,11,12,13]. A recent evaluation of the epidemiologic and laboratory findings by the International Agency for Research on Cancer (IARC) concluded that there was no substantial evidence of the carcinogenicity of carbon black in humans [14]. The sole finding of any serious outcome associated with toner exposure was a suggestion of an increased risk of sarcoidosis in African Americans [15]. This study was based on a relatively small study population (181 cases of sarcoidosis) and relied on self-reported subject exposure. A cross-sectional study of workers who handled toner found some increase in the prevalence of respiratory symptoms among exposed workers, which is consistent with the results from animal studies suggesting a mild to moderate inflammatory response at high exposure levels [16].

The Xerox Corporation initiated a retrospective cohort study of 34,147 U.S. Industrial Staff (i.e. manufacturing) and Service Engineers employed between 1960 and 1982 with the objective of evaluating any possible association between all-cause and cause-specific mortality and occupational toner exposure among Xerox employees. In the retrospective cohort design, a group is identified using historical records, e.g, employment records, and then their survival experience is tracked using various resources that provide information on vital status. The cohort investigated in this report was previously established and vital status was tracked through December 31, 1984 at which time 870 deaths had occurred. However, the follow-up time was not sufficient (average of less than 15 years) to reach any conclusions. Mortality rates were lower in those exposed to toner in comparison to the U.S. population; this pattern is not surprising since employed people tend to be healthier than the population in general, a phenomenon generally known as "the healthy worker effect" [17]. A subsequent analysis that tracked vital status through December 31, 1993 evaluated 2023 deaths over approximately 700,000 person-years of follow-up with an average of 22.3 years of follow-up among white males. Similar results were seen to those of the 1984 analysis with lower than expected death rates in the Xerox cohort compared to the U.S. population. In the toner exposed categories, only the rate for digestive cancers in the toner manufacturing subgroup of the exposed employees was higher than that of the general population[18] . However, the sub-group of this study population derived from Monroe County (Rochester), NY represents a disproportionate percentage of those engaged in toner manufacturing. The population in this geographic region of New York State also has a well-documented incidence and prevalence of digestive tract (especially colo-rectal) cancers that is in excess of the U.S. population as a whole. Thus, this finding may have been in part the result of higher rates of disease in the local population, from which Xerox draws its employees, relative to the US population.

In the present analyses, we used Xerox cohort data updated for employment history through December 31st, 1998 and vital status through December 31st, 1999. We report on the observed mortality of the employees who are classified as exposed to toner compared with a group of Xerox employees who were unexposed to toner. We compared overall and cause-specific mortality rates of exposed employees with age-, sex-, race- and calendar year-adjusted mortality rates from the US population. Last, to examine the presence of any healthy worker biases in the cohort, a period analysis was done examining observed and expected mortality differences as the cohort moved through various calendar periods.

METHODS

The study population consisted of the retrospective cohort assembled by the Occupational Health Information System Unit of the Xerox Corporation in the 1980s. The number of employees included in the study decreased to 33,671 as it was decided that 476 employees that were previously included did not fit the eligibility criteria (work at least 91 days in an exposure group). Three groups of employees at Xerox were considered eligible for the study if they had been employed for at least 91 consecutive days between January 1st, 1960 and December 31st, 1982: (1) toner manufacturing employees (TME) employed by Xerox in Oklahoma City, OK or in Monroe County (Rochester), NY; (2) hourly employees of Xerox in Monroe County identified as having no workplace exposure to toner; or (3) customer service engineers (CSE) employed by Xerox and based in the US. Employees who began employment as a supervisor, foreman, or engineer were not included in the study population. For additional details on the study methodology refer to the study protocol, The Retrospective Cohort Study of Mortality of Xerox Employees, authorized February 22, 2002 [19].

Toner exposure was determined based on work history records taken from Xerox employee databases, updated through the end of 1998. The toner exposed group consisted of CSE and TME while the unexposed group included the hourly employees from Monroe County who were not involved with toner manufacturing. Exposure status was classified through the end of 1982 from various employee records, including IRS941A wage lists, job history, union cards, and medical records. This exposure status was updated using a computerized employee database containing work history (budget center, job codes, status codes and building numbers) through the end of 1998. Some individuals who worked from 1960-1966 had incomplete employee records available for exposure categorization and were considered to have missing exposure histories.

Time at risk was apportioned to the appropriate exposure group once an individual had been working in a given capacity for 91 days. Follow-up began three months after employment or January 1, 1960, whichever was later. Participants could contribute time to both exposed and unexposed groups if exposed time followed unexposed time. Vital status through December 31st 1999 was ascertained through the National Death Index and/or the Social Security Master Death File with cause of death obtained through NDI Plus services, requested death certificates or from Xerox Benefit group records. Causes of death were reported as either International Classification of Diseases, version 9 (ICD9) or version 10 (ICD10) codes with the later converted to ICD9 before analysis. Individuals not reported dead were assumed to be alive up to the end of ascertainment.

Statistical Analysis. To examine the association between toner exposure and various demographic characteristics of the Xerox cohort, employees were stratified by gender (male, female), race (white, non-white) and exposure (exposed, unexposed). Given the high proportion of white and male employees among those with known race and gender, those with missing race were assumed to be white and those with missing gender information were assumed to be male. Subgroups of exposure based on employment capacity (TME, CSE) and location of employment (OKC, WEB) were also examined. The distribution of deaths among categories defined by these demographic factors and exposure was evaluated and crude estimates of the incidence rate of all-cause mortality were calculated. The overall survival experience of the controls and exposed employees was described using Kaplan Meier survival function estimates. The effect of age on mortality was accounted for by using age as the time axis for assessing survival. Thus, the survival in the exposed and unexposed could be compared for employees of equivalent ages.

Using estimates of the cause-specific mortality rate from the US population for 23 categories of causes of death, we computed standardized mortality ratios (SMRs) adjusted for age, sex, race and calendar year. Reference mortality rates for the period of 1979 through 1999 were obtained from the Centers for Disease Control (CDC) using the CDC Wonder mortality statistics request system. Reference mortality rates for the period of 1960 though 1978 were obtained using the tabulated data files from National Center for Health Statistics (NCHS). For 10 specific cancer diagnoses (esophagus, stomach, colon, rectum, liver, pancreas, prostate, testis, kidney and bladder) rates were not available for the years 1960-1978. Rates for the 10 cancer categories were interpolated for those years using the proportional change in the rate for the nearest available cancer category. Confidence intervals were calculated based upon exact Poisson probabilities using the method of Breslow and Day [20]. The categories of cause of death were chosen to mirror previous reports from the Xerox Mortality Study. A listing of the International Classification of Diseases, version 9 and version 10 codes, used to group causes is given in Appendix A. The SMR analysis provided a standardized external comparison for evaluating whether the rate of death from various causes in the Xerox cohort was higher or lower than that expected for the US population.

No adjustments were made for multiple comparisons in the calculation of the confidence intervals (calculated to provide nominal 95 % coverage of the true value as per standard frequentist statistical theory). In other words, because multiple tests of statistical significance were carried out, there is the possibility that some associations arose by chance alone. However, we note that for our SMR calculations, we compute confidence intervals for 23 SMR analyses (for all-cause, all-cancer, and individual cause-specific mortality outcomes) for 28 different groups and subgroups (defined by sex-, race-, exposure-, and location-criteria). A conservative approach for evaluating the evidence for any SMR estimate being statistically different from 1.0 is a Bonferroni correction that would require testing each at a $0.05/644 = 7.7 \times 10^{-5}$ level. We chose to use less stringent criteria, applying an alternative method for controlling the overall *false-discovery rate* (FDR). The Benjamini-Hochberg (B-H) approach accomplishes control of the FDR by comparing the observed p value in sequential order (from largest to smallest) to a list of critical values. The first value is the overall Type I error rate ($\alpha/2$ for two-sided testing); the last value is the Bonferroni critical value and all of the other p values are compared to statistical thresholds between the two values. We utilized this approach in evaluating the statistical significance of the 644 SMR values.

To evaluate the presence and extent of a healthy worker effect, the cumulative cohort follow-up was truncated at December 31st, 1987, 1990, 1993, 1996 and 1999 for all causes of mortality for the white males only. The healthy worker effect would be expected to lead to a pattern of reduced risk in the Xerox workers in comparison with the general population that would be lower at the successive follow-up intervals.

An additional analysis was also performed to assess the degree to which assumptions concerning pre-1979 cancer rates affected the SMR estimates. The SMR analysis was rerun using only person-time and events after 1979.

RESULTS

The Xerox cohort available for analysis consisted of 33,671 individuals with greater than 90 days of employment in a given exposure group between January 1, 1960 and December 31, 1982. Because participant age was needed for interpreting and comparing cause-specific mortality rates, 1,705 participants with unknown dates of birth were excluded, leaving a study population of 31,966. Additional information on race, gender and exposure was missing for the majority of the excluded participants (Table 1).

Of those remaining, 88 % were male and 67 % were white. Information on race was missing from the Xerox record for 5,217 (16 %) and for the purposes of the analysis they were assumed to be white; 162 (1 %) had no information on gender and were assumed to be male; and 467 (2 %) had no information on exposure and were placed in the unknown exposure group.

Approximately two thirds of the study population was exposed to toner either as a Customer Service Engineer (CSE) or in manufacturing while employed at Xerox. Over 95 % of the exposed employees were CSEs. Of the 878 employees working as toner manufacturing employees (TME), 83 % worked at the Webster plant (WEB) while the remainder worked at the Oklahoma City plant (OKC). Table 2 highlights the distribution of race and gender across the study population; Table 3 shows the distribution of race/gender groups across exposure groups; and Table 4 compares demographics, including age, across the exposure groups. The median age of the WEB and control groups at entry into the cohort (29 and 27 years, respectively) was greater than the median age of the CSE and OKC exposure groups (25 and 26 years, respectively). In addition, the interquartile ranges for the WEB and control groups were wider (24 - 40 for WEB; 22 - 38 for controls) than the CSE and OKC groups (23-28 for CSE; 23-33 for OKC).

After exclusions there were 3,374 deaths available for analysis occurring over 832,064 person-years of follow-up time with an average time of 26 years. Tables 5 and 6 present the number of deaths and person-time observed amongst the different exposure groups. Table 7 presents the crude death rates (i.e. unadjusted) across exposure groups. Figure 1 presents the overall cohort survival estimates plotted as a function of participant age; the curves show that the survival experience of the overall exposed group is slightly better across all ages compared to that of the control group.

SMR analysis

The SMR analysis compares the observed event (death) count to an expected number of events given US population mortality rates among a number of major disease and cancer types. These analyses are age-, sex-, race- and calendar year-adjusted and presented in entirety in Appendix B.

Table 8 summarizes the SMRs for all-cause, all-cancer, lung cancer, respiratory disease and cardiovascular disease mortality among the four sex/race groups who were exposed to toner. The SMR estimates for all-cause mortality in each of the four groups were less than 1.0 and the 95 % confidence intervals for the two male groups did not include 1.0. These estimates and their associated confidence limits indicate that the mortality experienced by each of these groups was no different (if not slightly better) than the mortality expected from the general population as anticipated based on the healthy worker effect.

Similar results were found for all-cancer, lung cancer, respiratory disease and cardiovascular disease SMR estimates for the two exposed male groups. For the two female exposed groups, the confidence intervals for the all-cancer, lung cancer, respiratory and cardiovascular disease estimates were generally wide due to the small number of events. Estimated 95 % confidence intervals included 1.0 for all the mortality categories except cardiovascular disease, for which the SMR estimate was significantly below 1.0. The data were consistent with no statistically significant increase in all cancer, lung cancer, respiratory and cardiovascular disease mortality among these groups.

There were SMR estimates for some mortality causes that were above 1.0. However, the confidence intervals for most of the estimates among the four exposed sex- and race-groups included 1.0. The exceptions were 9 statistically significant (<0.05) SMR estimates for cancers of the prostate (non-white male TME group), lung (all eligible white females and white female control group), stomach (white male control group), rectum and digestive system (all eligible white males and white male controls) and all cancers (white male OKC). Utilizing the B-H approach, these p-values would not attain the B-H critical values that would provide evidence against the null hypothesis for an SMR of 1.0.

The analysis evaluating the impact of assumptions made for pre-1979 cancer rates that were unavailable from the CDC or NCHS indicated that estimates were robust. When the study was anchored at 1979, minimal changes were noted in the SMRs. The largest discrepancy was in stomach and colon cancer SMR estimates, particularly in the female groups. The estimates were attenuated using only post-1979 person-time as a result of a majority of events occurring prior to that date.

DISCUSSION

Previous reports from this ongoing "Xerox Mortality Study" have suggested that toner exposure in this cohort does not increase the risk of mortality overall or in any of the disease categories evaluated. This report, using data updated for vital statistics through December 31st, 1999, supports previous results.

In general, there was a pattern of lower mortality in the Xerox population than expected compared to US mortality rates. The SMR for all causes were 0.65 and 0.88 for the white male exposed and control populations, respectively; 0.84 and 0.9 for white females exposed and control populations, respectively; 0.37 and 0.67 for non-white males, respectively; and 0.74 and 0.72 for non-white females, respectively. In addition, the SMRs for all cancers, lung cancer, respiratory disease and cardiovascular disease in white and non-white males were all lower than 1.0 in the toner-exposed population with the confidence limits not including 1.0 suggesting that there is no evidence that toner increases the risk of mortality in the Xerox population. This suggests that exposure to toner in an occupational setting does not cause an increase in mortality due to cancer, respiratory disease or cardiovascular disease.

The fact that the majority of the SMR estimates were below 1.0 for the Xerox populations is consistent with the "healthy worker effect" found in the two previous analyses. The healthy worker effect is the phenomenon whereby workers typically have overall death rates lower than those in the general population due to the severely ill or disabled being excluded from the workforce [21,22]. However, one would expect this effect to diminish as the study population ages and leaves the workforce. This can be examined in this study by looking at snapshots of these data over time. Table 9 shows the all-cause mortality in white males at 5 different time points (1987, 1990, 1993, 1996 and 1999). With progressively longer follow-up, the SMR estimates for all-cause mortality in white males, although still lower than 1.0, were increasingly attenuated (towards 1.0) in all groups, but OKC. The estimates for exposed white males changed from 0.48 (95% CI: 0.43, 0.53) in 1987 to 0.65 (95% CI: 0.61, 0.69) by 1999. Similar trends in SMR estimates with increasing follow-up time were seen in the SMRs for the unexposed group and for most subgroups of the exposed (Table 9).

There was some suggestion in the control group of higher rates of digestive cancers including cancers of the stomach and rectum. Statistically significant SMR estimates above 1.0 were found for stomach cancer in particular in the two earlier Xerox mortality studies, indicating that Xerox employees in the control group experienced higher risk of stomach cancer than the general US population. Because the control group was composed of hourly workers from Monroe County, we can compare the rate of stomach cancer in the control group with a reference rate drawn from the New York area. The National Cancer Institute provides cancer mortality rates that suggest a higher risk of digestive cancers in Monroe County and New York State in general compared to the US. If we apply the higher Monroe-county specific rates as reference, the crude SMR for stomach cancer in the white male control group becomes 0.92, down from the 1.00 using the US population reference rate. Similarly, the crude SMR estimate for rectal cancer in the white male control group drops from 1.13 to 0.83. The larger SMR estimates for digestive cancers in the Xerox cohort are, therefore, likely an artifact of the choice of reference rates (national versus state-specific) that do not adequately reflect the higher mortality from these cancers generally in the local population, possibly due to a large immigrant population. A case-control study was conducted following the initial analysis of the Xerox mortality data to evaluate the country of origin as a risk factor in the increase in digestive cancers in the control group. Overall, the conclusion from this case control study was that there was a significant association between Eastern European origin and the risk of death from digestive cancer[23].

In the previous analysis, a statistically significant increase in digestive cancers was also found in the white male TME group (SMR= 2.85; 95% CI= 1.23, 5.63). However, due to the small number of cases (8) and the diversity of types of cancers (esophagus (1), colon (2), liver (1), gallbladder (1), pancreas (2) and stomach (1)), the increase was considered as probably due to causes other than occupational exposure. In this current analysis, the SMR for digestive cancers in the white male TME group although still greater than one (SMR= 1.96; 95% CI= 0.84, 3.85) includes 1.0 in the confidence interval.

Significant results were also found for all-cancer in the OKC white males, prostate cancer in the TME non-white males and lung cancer in the control white females, indicating higher than expected mortality rates compared to the general US population. The all-cancer and prostate cancer SMR estimates were generated from only 5 and 2 events in 1,862 and 2,640 person-years of follow-up, respectively. The OKC and TME groups were both relatively small subsamples of the exposed group and consequently great caution is needed in interpreting these findings. These results were not consistent across race/gender groups or across exposure groups suggesting that these findings are likely due to chance. Given an expected Type I statistical error rate of 5%, 644 comparisons would yield 32 false positives by chance alone. The BH p-value correction to account for multiple comparisons is appropriate for these comparisons and diminishes the significance to a level not inconsistent with a hypothesis of no increased cancer rate. In contrast the lung cancer findings in the control white females result from 39 events in 44,454 person-years of follow-up. Any extant effects of toner exposure would be expected to result in diseases of the respiratory system such as chronic obstructive pulmonary disease (COPD) and lung cancer. These results, however, come from the unexposed members of the cohort and are not echoed in any of the exposure groups as evidenced by the SMR estimate of 0.66 (95% CI: 0.08,2.38) for exposed white females. Higher rates of lung cancer may be the result of smoking behavior in the control white females, which could not be assessed in this study.

These findings need to be interpreted within the constraints of this study design and of the data available. The limitations of occupational mortality studies are well characterized and include: 1) use of a health outcome indicator, mortality and cause-of-death, that is not highly sensitive to effects of occupational exposures and subject to misclassification; 2) use of internal and external control populations that may not match the exposed population on key characteristics; and 3) lack of information on key potential confounding or modifying factors, such as cigarette smoking. Statistical power was also limited within particular subgroups, particularly for women and non-whites.

CONCLUSION AND RECOMMENDATIONS

In conclusion, this analysis evaluated 3,374 mortality events occurring over 832,064 person-years of follow-up time (average follow-up time 26 years). The results of this analysis are consistent with the general mortality patterns among healthy working populations. We found no evidence that toner exposure increases the risk of all-cause mortality, or for cause-specific mortality for 23 categories of cause of death. However, follow-up of the cohort should be maintained with a repeated assessment of mortality patterns as the population continues to age.

FIGURES AND TABLES

Table 1. Comparison of eligible and excluded members of the Xerox Employee Cohort

	Eligible #	Eligible %	Excluded #	Excluded %
Non-White	5,461	17.1	3	0.2
White	21,288	66.6	5	0.3
Unknown race	5,217	16.3	1,697	99.5
Control+Exposed	544	1.7	1	0.1
Control	10,012	31.3	304	17.8
Exposed	20,943	65.5	297	17.4
Unknown exposure	467	1.5	1,103	64.7
Male	28,113	87.9	52	3.0
Female	3,691	11.5	5	0.3
Unknown gender	162	0.5	1,648	96.7
Total	31,966		1,705	

Table 2. Distribution of the eligible employees by race and gender

RACE	Male (%)	Female (%)	Unknown (%)	Total
Non-White	4,714 (16.8)	745 (20.2)	2 (1.2)	5,461
White	18,841(67.0)	2,446 (66.3)	1 (0.6)	21,288
Unknown	4,558 (16.2)	500 (13.5)	159 (98.1)	5,217
Total	28,113	3,691	162	31,966

Table 3. Distribution of race, sex and exposure among the eligible employees

	White Male	Non-White Male	White Female	Non-White Female	Total
Exposed	16,069 (74.8)	3,931 (18.3)	1,160 (5.4)	327 (1.5)	21,487
• CSE	15,465 (75.0)	3,798 (18.4)	1,073 (5.2)	278 (1.3)	20,614
• TME	608 (69.2)	134 (15.3)	87 (9.9)	49 (5.6)	878
- OKC	93 (62.0)	29 (19.3)	16 (10.7)	12 (8.0)	150
- WEB	516 (70.8)	105 (14.4)	71 (9.7)	37 (5.1)	729
Control	7,522 (71.3)	861 (8.2)	1,728 (16.4)	445 (4.2)	10,556
Unknown	344 (73.7)	5 (1.1)	113 (24.2)	5 (1.1)	467
Overall	23,559 (73.7)	4,716 (14.8)	2,946 (9.2)	745 (2.3)	31,966

Table 4. Comparison of exposure groups (CSE, TME and overall) to the control group and pay method unknown group across pertinent characteristics.

	Exposed	CSE	TME	OKC	WEB	Controls	Unknown
Overall	21,487	20,614	878	150	729	10,556	467
Gender							
Male	19,900	19,165	740	122	619	8,339	330
Female	1,487	1,351	136	28	108	2,173	118
Unknown	100	98	2	0	2	44	19
Race							
Non-White	4,258	4,076	183	41	142	1,306	10
White	14,522	13,851	675	109	567	7,020	167
Unknown	2,707	2,687	20	0	20	2,230	290
Year of Birth							
1890	1	1	0	0	0	21	3
1900	8	8	0	0	0	135	11
1910	62	42	20	1	19	822	17
1920	434	381	53	6	47	1,532	60
1930	3,030	2,901	130	18	112	2,165	194
1940	11,450	11,107	344	43	301	3,865	182
1950	6,221	5,900	323	80	244	1,881	0
1960	281	274	8	2	6	135	0
							Median (IQR*)
Age at entry into cohort (Years)	25 (23,29)	25 (23,28)	28 (23,39)	26 (23, 33)	29 (24,40)	27 (22,38)	24 (21,29)
NWF	26 (23,31)	25.5 (22,29)	34 (26,44)	28.5 (25,35)	39 (26,45)	27 (23,34)	22 (22,33)
NWM	26 (23,30)	26 (23,29)	28.5 (23,38)	26 (23,33)	30 (24,39)	26 (22,33)	23 (21,24)
WF	26 (23,30)	26 (23,30)	35 (25,47)	31 (25,36.5)	38 (25,51)	35 (25,44)	22 (19,28)
WM	25 (23,28)	25 (23,28)	27 (23,37)	26 (23,31)	28 (23,37.5)	26 (21,36)	25 (21.5,30)

*IQR = Interquartile Range, 25th and 75th percentiles

Table 5. The distribution of deaths in the study population across race, gender and exposure categories

	White Male	Non-White Male	White Female	Non-white Female	Total
Exposed	1,104 (80.6)	217 (15.9)	36 (2.6)	12 (0.9)	1,369
CSE	1,044 (81.2)	199 (15.5)	32 (2.5)	11 (0.9)	1,286
TME	60 (72.3)	18 (21.7)	4 (4.8)	1 (1.2)	83
OKC	11 (68.8)	4 (25.0)	0	1 (6.3)	16
Webster	49 (73.1)	14 (20.9)	4 (6.0)	0	67
Controls	1,495 (75.9)	144 (7.3)	292 (14.8)	39 (2.0)	1,970
Unknown	74 (86.0)	0	11 (12.8)	1 (1.2)	86
Overall	2,635 (78.1)	352 (10.4)	335 (9.9)	52 (1.5)	3,374

Table 6. The distribution of person years across the exposure categories by race and gender

	White Male	Non-White Male	White Female	Non-White Female
Exposed	422,264	89,513	23,924	6,160
-CSE	409,420	86,889	22,233	5,350
-TME	12,890	2,639	1,692	810
-OKC	1,862	578	311	247
-WEB	11,030	2,061	1,381	563
Control	199,019	20,169	44,454	10,627
Unknown	11,405	174	3,908	157
Overall	632,889	109,892	72,330	16,953

Table 7. Crude death rates across exposure groups among race and gender groups (per 1000 person years)

	White Male	Non-White Male	White Female	Non-White Female
Exposed	2.61	2.42	1.50	1.95
-CSE	2.55	2.29	1.44	2.06
-TME	4.65	6.82	2.36	1.23
-OKC	5.91	6.92	0.00	4.04
-WEB	4.44	6.79	2.90	0.00
Control	7.51	7.14	6.57	3.67
Unknown	6.49	0.00	2.81	6.37
Overall	4.16	3.20	4.63	3.07

Figure 1. Overall Survival Estimates (Control versus Exposed Employees) – all gender/race groups

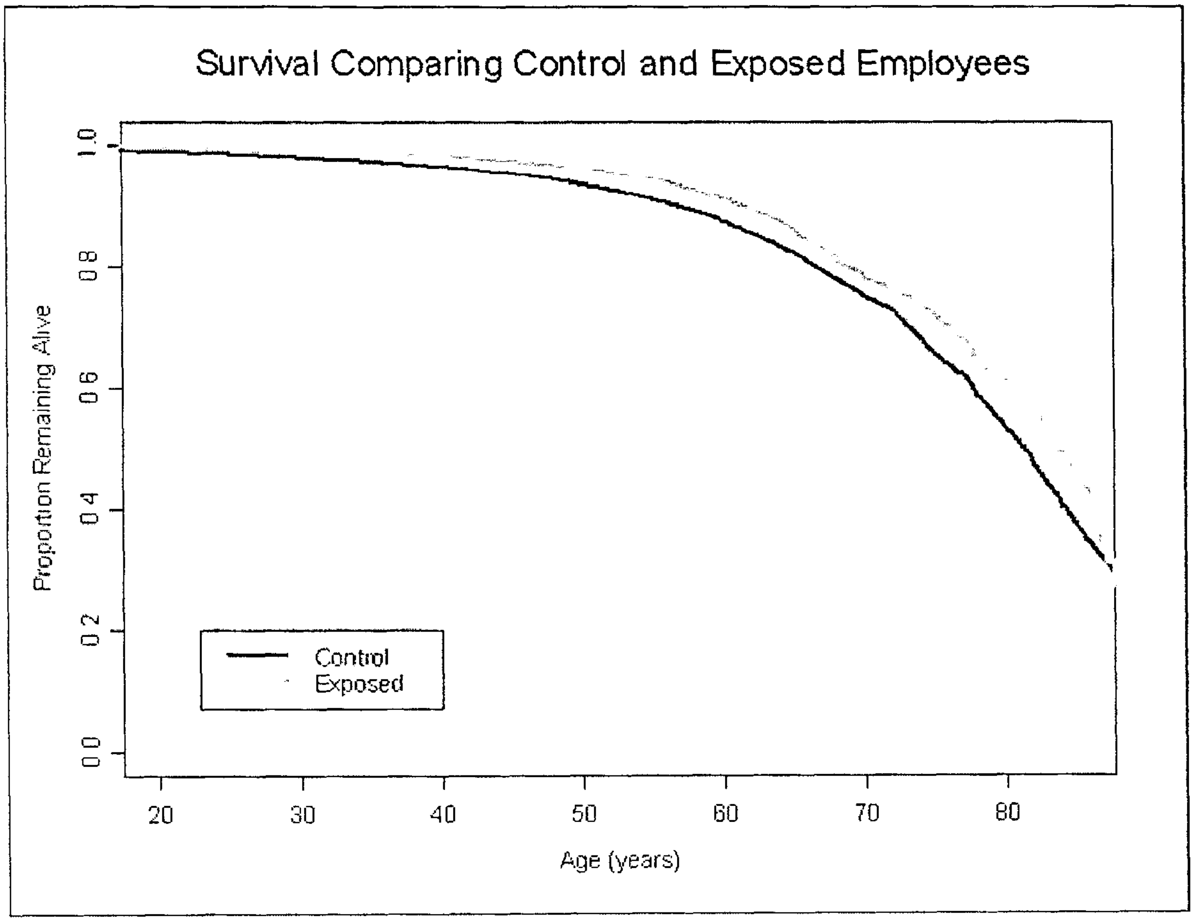

Figure 1. Estimated survival curves over age in the exposed to the control group

Table 8: Summary of SMR results (with 95% confidence intervals) for all-cause, all-cancer, lung cancer, respiratory disease and cardiovascular disease mortality among exposed Xerox employees

Table	Group	All-Cause SMR	All-cancer SMR	Lung Cancer SMR
B2	White Males	0.65 (0.61, 0.69)	0.81 (0.72, 0.90)	0.64 (0.51, 0.79)
B9	Non-white Males	0.37 (0.32, 0.42)	0.56 (0.42, 0.73)	0.47 (0.26, 0.77)
B16	White Females	0.84 (0.59, 1.16)	1.01 (0.58, 1.64)	0.66 (0.08, 2.38)
B23	Non-white Females	0.74 (0.38, 1.28)	0.98 (0.27, 2.51)	1.64 (0.04, 9.14)

Table	Group	Respiratory Disease	Cardiovascular Disease
B2	White Males	0.67 (0.45, 0.95)	0.65 (0.59, 0.73)
B9	Non-white Males	0.35 (0.09, 0.89)	0.41 (0.31, 0.52)
B16	White Females	_	0.2 (0.02, 0.73)
B23	Non-white Females	4.48 (0.54, 16.18)	0.24 (0.01, 1.32)

Table 9. SMR analysis for all-cause mortality in white males using cumulative data up to 5 different years when the data are administratively censored.

Censoring Year	All Cause SMR estimate (95% CI)						
				Exposed Group			
	Eligible	Exposed	Control	CSE	TME	OKC	Webster
1987	0.64 (0.60,0.68)	0.48 (0.43,0.53)	0.76 (0.70,0.82)	0.48 (0.42,0.53)	0.48 (0.25,0.84)	1.16 (0.24,3.39)	0.40 (0.18,0.76)
1990	0.65 (0.62,0.69)	0.49 (0.45,0.54)	0.78 (0.72,0.83)	0.49 (0.45,0.54)	0.46 (0.26,0.75)	1.42 (0.46,3.31)	0.35 (0.18,0.63)
1993	0.67 (0.64,0.71)	0.54 (0.50,0.58)	0.78 (0.74,0.84)	0.53 (0.49,0.58)	0.64 (0.43,0.92)	1.29 (0.47,2.81)	0.57 (0.37,0.85)
1996	0.70 (0.67,0.73)	0.56 (0.52,0.60)	0.81 (0.77,0.86)	0.56 (0.52,0.60)	0.68 (0.49,0.92)	0.98 (0.36,2.12)	0.64 (0.45,0.89)
1999	0.77 (0.74,0.80)	0.65 (0.61,0.69)	0.88 (0.83,0.93)	0.64 (0.60,0.68)	0.85 (0.65,1.10)	1.52 (0.76,2.72)	0.77 (0.57,1.02)

APPENDIX A: ICD9 AND ICD10 CODES USED FOR CATEGORIZATION OF OUTCOMES

Outcome	ICD9 code	ICD10 code	notes
Digestive Cancer	150-159	C15-C26	
Esophageal Cancer	150	C15	
Stomach Cancer	151	C16	
Colon Cancer	153	C18	
Cancer of the Rectum	154.1	C20	Does not include cancer of the rectosigmoid junction
Liver Cancer	155	C22	
Pancreatic Cancer	157	C25	
Lung Cancer	162	C34	
Skin Cancer	172	C43	Only includes melanoma
Breast Cancer	174	C50	
Prostate Cancer	185	C61	
Testicular Cancer	186	C62	
Bladder Cancer	!88	C67	
Kidney Cancer	189	C64	
Brain Cancer	191	C71	
Leukemia	204-208	C91-C95	
Lymphomas and Multiple Myelomas	200-203	C81-C90, C96	
Diabetes	250	E10-E14	
Cardiovascular Disease	390-459	I00-I99	
Respiratory Disease	470-478, 490-519	J30-J98	
All Cancer	140-208	C00-C97	
All External Causes	E800-E999	V01-Y98	

APPENDIX B: SMR TABLES OF SMR FOR EACH CAUSE OF DEATH FOR EACH RACE AND GENDER GROUP

Table B1. SMR analysis results for eligible white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	31	23.95	632611.17	1.29	(0.88,1.84)
Cancer of the stomach	31	24.27	632611.17	1.28	(0.87,1.81)
Cancer of the colon	69	66.27	632611.17	1.04	(0.81,1.32)
Cancer of the rectum	21	11.34	632611.17	1.85	(1.15,2.83)
Cancer of the liver	8	16.42	632611.17	0.49	(0.21,0.96)
Cancer of the pancreas	51	40	632611.17	1.28	(0.95,1.68)
Cancer of the lung	243	290.68	632611.17	0.84	(0.73,0.95)
Cancer of the skin	33	23.43	632611.17	1.41	(0.97,1.98)
Cancer of the breast	0	0.1	632611.17	.	
Cancer of the bladder	21	15.6	632611.17	1.35	(0.83,2.06)
Cancer of the testis	3	4.44	632611.17	0.68	(0.14,1.97)
Cancer of the prostate	41	41.93	632611.17	0.98	(0.7,1.33)
Cancer of the kidney	21	24.1	632611.17	0.87	(0.54,1.33)
Cancer of the brain	27	32.41	632611.17	0.83	(0.55,1.21)
Leukemia	35	34.6	632611.17	1.01	(0.7,1.41)
Lymphomas and multiple myelomas	47	58.2	632611.17	0.81	(0.59,1.07)
Diabetes	35	63.47	632611.17	0.55	(0.38,0.77)
Cardiovascular disease	933	1224.69	632611.17	0.76	(0.71,0.81)
Respiratory disease	102	126.64	632611.17	0.81	(0.66,0.98)
All external	381	526.48	632611.17	0.72	(0.65,0.8)
All cancer	783	828.99	632611.17	0.94	(0.88,1.01)
All causes	2635	3419.39	632611.17	0.77	(0.74,0.8)
Cancer of the digestive system	227	194.24	632611.17	1.17	(1.02,1.33)

Table B2: SMR analysis results for exposed white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	14	11.83	421966.87	1.18	(0.65,1.99)
Cancer of the stomach	10	11.32	421966.87	0.88	(0.42,1.62)
Cancer of the colon	29	29.43	421966.87	0.99	(0.66,1.42)
Cancer of the rectum	7	5.19	421966.87	1.35	(0.54,2.78)
Cancer of the liver	6	8.22	421966.87	0.73	(0.27,1.59)
Cancer of the pancreas	24	18.67	421966.87	1.29	(0.82,1.91)
Cancer of the lung	84	132.15	421966.87	0.64	(0.51,0.79)
Cancer of the skin	19	14.03	421966.87	1.35	(0.82,2.11)
Cancer of the breast	0	0.01	421966.87	.	
Cancer of the bladder	7	5.89	421966.87	1.19	(0.48,2.45)
Cancer of the testis	0	3	421966.87	.	
Cancer of the prostate	9	11.9	421966.87	0.76	(0.35,1.44)
Cancer of the kidney	10	12.22	421966.87	0.82	(0.39,1.51)
Cancer of the brain	12	18.86	421966.87	0.64	(0.33,1.11)
Leukemia	18	17.76	421966.87	1.01	(0.6,1.6)
Lymphomas and multiple myelomas	22	30.67	421966.87	0.72	(0.45,1.09)
Diabetes	15	32.04	421966.87	0.47	(0.26,0.77)
Cardiovascular disease	342	524.22	421966.87	0.65	(0.59,0.73)
Respiratory disease	31	46.39	421966.87	0.67	(0.45,0.95)
All external	225	348.85	421966.87	0.64	(0.56,0.73)
All cancer	316	391.09	421966.87	0.81	(0.72,0.9)
All causes	1104	1698.26	421966.87	0.65	(0.61,0.69)
Cancer of the digestive system	96	90.14	421966.87	1.06	(0.86,1.3)

Table B3: SMR analysis results for control white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	17	11.47	199018.74	1.48	(0.86,2.37)
Cancer of the stomach	21	12.3	199018.74	1.71	(1.06,2.61)
Cancer of the colon	38	35.04	199018.74	1.08	(0.77,1.49)
Cancer of the rectum	13	5.85	199018.74	2.22	(1.18,3.8)
Cancer of the liver	2	7.78	199018.74	0.26	(0.03,0.93)
Cancer of the pancreas	24	20.24	199018.74	1.19	(0.76,1.76)
Cancer of the lung	146	150.33	199018.74	0.97	(0.82,1.14)
Cancer of the skin	13	8.87	199018.74	1.47	(0.78,2.51)
Cancer of the breast	0	0.08	199018.74	.	
Cancer of the bladder	14	9.27	199018.74	1.51	(0.83,2.53)
Cancer of the testis	2	1.36	199018.74	1.48	(0.18,5.33)
Cancer of the prostate	28	28.83	199018.74	0.97	(0.65,1.4)
Cancer of the kidney	11	11.25	199018.74	0.98	(0.49,1.75)
Cancer of the brain	14	12.8	199018.74	1.09	(0.6,1.84)
Leukemia	17	15.99	199018.74	1.06	(0.62,1.7)
Lymphomas and multiple myelomas	25	26.1	199018.74	0.96	(0.62,1.41)
Diabetes	20	29.82	199018.74	0.67	(0.41,1.04)
Cardiovascular disease	558	666.89	199018.74	0.84	(0.77,0.91)
Respiratory disease	67	76.75	199018.74	0.87	(0.68,1.11)
All external	147	168.54	199018.74	0.87	(0.74,1.03)
All cancer	437	415.69	199018.74	1.05	(0.95,1.15)
All causes	1438	1636.56	199018.74	0.88	(0.83,0.93)
Cancer of the digestive system	123	98.85	199018.74	1.24	(1.03,1.48)

Table B4: SMR analysis results for CSE white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	13	11.32	409152.93	1.15	(0.61,1.96)
Cancer of the stomach	9	10.82	409152.93	0.83	(0.38,1.58)
Cancer of the colon	27	28.03	409152.93	0.96	(0.63,1.4)
Cancer of the rectum	7	4.95	409152.93	1.41	(0.57,2.91)
Cancer of the liver	5	7.86	409152.93	0.64	(0.21,1.49)
Cancer of the pancreas	22	17.83	409152.93	1.23	(0.77,1.87)
Cancer of the lung	79	125.96	409152.93	0.63	(0.5,0.78)
Cancer of the skin	19	13.55	409152.93	1.4	(0.84,2.19)
Cancer of the breast	0	0.01	409152.93	.	
Cancer of the bladder	7	5.55	409152.93	1.26	(0.51,2.6)
Cancer of the testis	0	2.92	409152.93	.	
Cancer of the prostate	9	10.95	409152.93	0.82	(0.38,1.56)
Cancer of the kidney	9	11.71	409152.93	0.77	(0.35,1.46)
Cancer of the brain	11	18.2	409152.93	0.6	(0.3,1.08)
Leukemia	18	17.04	409152.93	1.06	(0.63,1.67)
Lymphomas and multiple myelomas	21	29.45	409152.93	0.71	(0.44,1.09)
Diabetes	14	30.7	409152.93	0.46	(0.25,0.77)
Cardiovascular disease	320	499.73	409152.93	0.64	(0.57,0.71)
Respiratory disease	29	43.56	409152.93	0.67	(0.45,0.96)
All external	217	337.79	409152.93	0.64	(0.56,0.73)
All cancer	299	373.56	409152.93	0.8	(0.71,0.9)
All causes	1044	1627.89	409152.93	0.64	(0.6,0.68)
Cancer of the digestive system	88	86.06	409152.93	1.02	(0.82,1.26)

Table B5: SMR analysis results for TME white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	0.51	12879.46	1.95	(0.05,10.85)
Cancer of the stomach	1	0.5	12879.46	1.99	(0.05,11.11)
Cancer of the colon	2	1.4	12879.46	1.43	(0.17,5.18)
Cancer of the rectum	0	0.23	12879.46	.	
Cancer of the liver	1	0.36	12879.46	2.78	(0.07,15.49)
Cancer of the pancreas	2	0.84	12879.46	2.38	(0.29,8.6)
Cancer of the lung	5	6.19	12879.46	0.81	(0.26,1.88)
Cancer of the skin	0	0.48	12879.46	.	
Cancer of the breast	0	0	12879.46	.	
Cancer of the bladder	0	0.34	12879.46	.	
Cancer of the testis	0	0.08	12879.46	.	
Cancer of the prostate	0	0.95	12879.46	.	
Cancer of the kidney	1	0.5	12879.46	1.99	(0.05,11.07)
Cancer of the brain	1	0.67	12879.46	1.5	(0.04,8.34)
Leukemia	0	0.72	12879.46	.	
Lymphomas and multiple myelomas	1	1.22	12879.46	0.82	(0.02,4.58)
Diabetes	1	1.35	12879.46	0.74	(0.02,4.13)
Cardiovascular disease	22	24.52	12879.46	0.9	(0.56,1.36)
Respiratory disease	2	2.84	12879.46	0.7	(0.09,2.54)
All external	8	11.12	12879.46	0.72	(0.31,1.42)
All cancer	17	17.55	12879.46	0.97	(0.56,1.55)
All causes	60	70.53	12879.46	0.85	(0.65,1.1)
Cancer of the digestive system	8	4.09	12879.46	1.96	(0.84,3.85)

Table B6

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Table B7

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Table B8: SMR analysis results for eligible non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	2	7.98	109881.45	0.25	(0.03,0.91)
Cancer of the stomach	5	6.18	109881.45	0.81	(0.26,1.89)
Cancer of the colon	8	9.51	109881.45	0.84	(0.36,1.66)
Cancer of the rectum	0	1.68	109881.45	.	
Cancer of the liver	2	5.98	109881.45	0.33	(0.04,1.21)
Cancer of the pancreas	8	6.18	109881.45	1.29	(0.56,2.55)
Cancer of the lung	24	47.19	109881.45	0.51	(0.33,0.76)
Cancer of the skin	0	0.25	109881.45	.	
Cancer of the breast	0	0	109881.45	.	
Cancer of the bladder	0	1.2	109881.45	.	
Cancer of the testis	1	0.21	109881.45	4.86	(0.12,27.07)
Cancer of the prostate	6	7.24	109881.45	0.83	(0.3,1.8)
Cancer of the kidney	1	2.87	109881.45	0.35	(0.01,1.94)
Cancer of the brain	1	2.36	109881.45	0.42	(0.01,2.36)
Leukemia	4	4.46	109881.45	0.9	(0.24,2.3)
Lymphomas and multiple myelomas	5	8.16	109881.45	0.61	(0.2,1.43)
Diabetes	5	16.62	109881.45	0.3	(0.1,0.7)
Cardiovascular disease	115	218.43	109881.45	0.53	(0.43,0.63)
Respiratory disease	8	16.87	109881.45	0.47	(0.2,0.93)
All external	62	155.67	109881.45	0.4	(0.31,0.51)
All cancer	80	138.8	109881.45	0.58	(0.46,0.72)
All causes	352	789.61	109881.45	0.45	(0.4,0.49)
Cancer of the digestive system	26	39.19	109881.45	0.66	(0.43,0.97)

Table B9: SMR analysis results for exposed non- white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	5.54	89501.86	0.18	(0,1.01)
Cancer of the stomach	3	4.26	89501.86	0.7	(0.15,2.06)
Cancer of the colon	6	6.57	89501.86	0.91	(0.34,1.99)
Cancer of the rectum	0	1.19	89501.86	.	
Cancer of the liver	2	4.5	89501.86	0.44	(0.05,1.61)
Cancer of the pancreas	6	4.25	89501.86	1.41	(0.52,3.08)
Cancer of the lung	15	32.16	89501.86	0.47	(0.26,0.77)
Cancer of the skin	0	0.18	89501.86	.	
Cancer of the breast	0	0	89501.86	.	
Cancer of the bladder	0	0.74	89501.86	.	
Cancer of the testis	1	0.17	89501.86	5.84	(0.15,32.52)
Cancer of the prostate	5	3.68	89501.86	1.36	(0.44,3.17)
Cancer of the kidney	1	2.08	89501.86	0.48	(0.01,2.67)
Cancer of the brain	1	1.8	89501.86	0.56	(0.01,3.1)
Leukemia	4	3.31	89501.86	1.21	(0.33,3.1)
Lymphomas and multiple myelomas	2	6.03	89501.86	0.33	(0.04,1.2)
Diabetes	4	12.08	89501.86	0.33	(0.09,0.85)
Cardiovascular disease	62	152.38	89501.86	0.41	(0.31,0.52)
Respiratory disease	4	11.53	89501.86	0.35	(0.09,0.89)
All external	38	127.62	89501.86	0.3	(0.21,0.41)
All cancer	54	96.26	89501.86	0.56	(0.42,0.73)
All causes	217	587.67	89501.86	0.37	(0.32,0.42)
Cancer of the digestive system	18	27.49	89501.86	0.65	(0.39,1.03)

Table B10: SMR analysis results for control non- white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	2.42	20169.27	0.41	(0.01,2.3)
Cancer of the stomach	2	1.91	20169.27	1.05	(0.13,3.78)
Cancer of the colon	2	2.93	20169.27	0.68	(0.08,2.47)
Cancer of the rectum	0	0.48	20169.27	.	
Cancer of the liver	0	1.47	20169.27	.	
Cancer of the pancreas	2	1.92	20169.27	1.04	(0.13,3.76)
Cancer of the lung	9	14.93	20169.27	0.6	(0.28,1.14)
Cancer of the skin	0	0.07	20169.27	.	
Cancer of the breast	0	0	20169.27	.	
Cancer of the bladder	0	0.46	20169.27	.	
Cancer of the testis	0	0.03	20169.27	.	
Cancer of the prostate	1	3.55	20169.27	0.28	(0.01,1.57)
Cancer of the kidney	0	0.78	20169.27	.	
Cancer of the brain	0	0.55	20169.27	.	
Leukemia	0	1.14	20169.27	.	
Lymphomas and multiple myelomas	3	2.12	20169.27	1.42	(0.29,4.14)
Diabetes	1	4.5	20169.27	0.22	(0.01,1.24)
Cardiovascular disease	53	65.63	20169.27	0.81	(0.6,1.06)
Respiratory disease	4	5.31	20169.27	0.75	(0.21,1.93)
All external	24	27.78	20169.27	0.86	(0.55,1.29)
All cancer	26	42.28	20169.27	0.62	(0.4,0.9)
All causes	135	200.38	20169.27	0.67	(0.56,0.8)
Cancer of the digestive system	8	11.63	20169.27	0.69	(0.3,1.36)

Table B11: SMR analysis results for CSE non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	5.35	86878.55	.	
Cancer of the stomach	3	4.12	86878.55	0.73	(0.15,2.13)
Cancer of the colon	6	6.34	86878.55	0.95	(0.35,2.06)
Cancer of the rectum	0	1.15	86878.55	.	
Cancer of the liver	2	4.35	86878.55	0.46	(0.06,1.66)
Cancer of the pancreas	6	4.1	86878.55	1.46	(0.54,3.19)
Cancer of the lung	14	31.03	86878.55	0.45	(0.25,0.76)
Cancer of the skin	0	0.17	86878.55	.	
Cancer of the breast	0	0	86878.55	.	
Cancer of the bladder	0	0.72	86878.55	.	
Cancer of the testis	1	0.17	86878.55	6.01	(0.15,33.47)
Cancer of the prostate	3	3.55	86878.55	0.85	(0.17,2.47)
Cancer of the kidney	1	2.01	86878.55	0.5	(0.01,2.77)
Cancer of the brain	1	1.74	86878.55	0.57	(0.01,3.2)
Leukemia	3	3.2	86878.55	0.94	(0.19,2.74)
Lymphomas and multiple myelomas	2	5.83	86878.55	0.34	(0.04,1.24)
Diabetes	3	11.68	86878.55	0.26	(0.05,0.75)
Cardiovascular disease	55	147.29	86878.55	0.37	(0.28,0.49)
Respiratory disease	4	11.15	86878.55	0.36	(0.1,0.92)
All external	37	123.97	86878.55	0.3	(0.21,0.41)
All cancer	48	92.94	86878.55	0.52	(0.38,0.68)
All causes	199	569.09	86878.55	0.35	(0.3,0.4)
Cancer of the digestive system	17	26.54	86878.55	0.64	(0.37,1.03)

Table B12: SMR analysis results for TME non-white males.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	1	0.2	2639.05	5.01	(0.13,27.93)
Cancer of the stomach	0	0.15	2639.05	.	
Cancer of the colon	0	0.23	2639.05	.	
Cancer of the rectum	0	0.04	2639.05	.	
Cancer of the liver	0	0.15	2639.05	.	
Cancer of the pancreas	0	0.15	2639.05	.	
Cancer of the lung	1	1.15	2639.05	0.87	(0.02,4.83)
Cancer of the skin	0	0.01	2639.05	.	
Cancer of the breast	0	0	2639.05	.	
Cancer of the bladder	0	0.03	2639.05	.	
Cancer of the testis	0	0	2639.05	.	
Cancer of the prostate	2	0.14	2639.05	14.72	(1.78,53.17)
Cancer of the kidney	0	0.07	2639.05	.	
Cancer of the brain	0	0.06	2639.05	.	
Leukemia	1	0.11	2639.05	9.39	(0.24,52.32)
Lymphomas and multiple myelomas	0	0.2	2639.05	.	
Diabetes	1	0.41	2639.05	2.44	(0.06,13.61)
Cardiovascular disease	7	5.17	2639.05	1.35	(0.54,2.79)
Respiratory disease	0	0.39	2639.05	.	
All external	1	3.67	2639.05	0.27	(0.01,1.52)
All cancer	6	3.37	2639.05	1.78	(0.65,3.88)
All causes	18	18.78	2639.05	0.96	(0.57,1.52)
Cancer of the digestive system	1	0.96	2639.05	1.04	(0.03,5.79)

Table B13

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Table B14

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Table B15: SMR analysis results for eligible white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	2	1.09	72329.83	1.83	(0.22,6.61)
Cancer of the stomach	3	2.3	72329.83	1.31	(0.27,3.82)
Cancer of the colon	7	10.78	72329.83	0.65	(0.26,1.34)
Cancer of the rectum	1	1.36	72329.83	0.74	(0.02,4.1)
Cancer of the liver	1	1.57	72329.83	0.64	(0.02,3.55)
Cancer of the pancreas	5	5.79	72329.83	0.86	(0.28,2.01)
Cancer of the lung	43	28.21	72329.83	1.52	(1.1,2.05)
Cancer of the skin	0	1.84	72329.83	.	
Cancer of the breast	31	27.12	72329.83	1.14	(0.78,1.62)
Cancer of the bladder	3	1.19	72329.83	2.52	(0.52,7.36)
Cancer of the testis	0	0	72329.83	.	
Cancer of the prostate	0	0	72329.83	.	
Cancer of the kidney	0	2.12	72329.83	.	
Cancer of the brain	1	3.38	72329.83	0.3	(0.01,1.65)
Leukemia	3	4	72329.83	0.75	(0.15,2.19)
Lymphomas and multiple myelomas	10	7.06	72329.83	1.42	(0.68,2.6)
Diabetes	3	10.43	72329.83	0.29	(0.06,0.84)
Cardiovascular disease	104	138.46	72329.83	0.75	(0.61,0.91)
Respiratory disease	20	19.78	72329.83	1.01	(0.62,1.56)
All external	30	20.92	72329.83	1.43	(0.97,2.05)
All cancer	132	127.51	72329.83	1.04	(0.87,1.23)
All causes	335	383.09	72329.83	0.87	(0.78,0.97)
Cancer of the digestive system	19	25.27	72329.83	0.75	(0.45,1.17)

Table B16: SMR analysis results for exposed white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.09	23924.45	.	
Cancer of the stomach	0	0.24	23924.45	.	
Cancer of the colon	1	0.98	23924.45	1.02	(0.03,5.66)
Cancer of the rectum	0	0.13	23924.45	.	
Cancer of the liver	0	0.18	23924.45	.	
Cancer of the pancreas	0	0.51	23924.45	.	
Cancer of the lung	2	3.04	23924.45	0.66	(0.08,2.38)
Cancer of the skin	0	0.39	23924.45	.	
Cancer of the breast	6	4.23	23924.45	1.42	(0.52,3.09)
Cancer of the bladder	0	0.09	23924.45	.	
Cancer of the testis	0	0	23924.45	.	
Cancer of the prostate	0	0	23924.45	.	
Cancer of the kidney	0	0.24	23924.45	.	
Cancer of the brain	0	0.58	23924.45	.	
Leukemia	0	0.59	23924.45	.	
Lymphomas and multiple myelomas	1	0.83	23924.45	1.21	(0.03,6.72)
Diabetes	0	1.11	23924.45	.	
Cardiovascular disease	2	9.87	23924.45	0.2	(0.02,0.73)
Respiratory disease	0	1.6	23924.45	.	
All external	10	6.39	23924.45	1.56	(0.75,2.88)
All cancer	16	15.83	23924.45	1.01	(0.58,1.64)
All causes	36	42.97	23924.45	0.84	(0.59,1.16)
Cancer of the digestive system	1	2.36	23924.45	0.42	(0.01,2.36)

Table B17: SMR analysis results for control white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	2	0.95	44453.52	2.1	(0.25,7.57)
Cancer of the stomach	3	1.94	44453.52	1.55	(0.32,4.53)
Cancer of the colon	6	9.25	44453.52	0.65	(0.24,1.41)
Cancer of the rectum	1	1.15	44453.52	0.87	(0.02,4.83)
Cancer of the liver	1	1.32	44453.52	0.76	(0.02,4.23)
Cancer of the pancreas	5	5.01	44453.52	1	(0.32,2.33)
Cancer of the lung	39	23.97	44453.52	1.63	(1.16,2.22)
Cancer of the skin	0	1.35	44453.52	.	
Cancer of the breast	24	21.58	44453.52	1.11	(0.71,1.65)
Cancer of the bladder	3	1.04	44453.52	2.89	(0.6,8.44)
Cancer of the testis	0	0	44453.52	.	
Cancer of the prostate	0	0	44453.52	.	
Cancer of the kidney	0	1.79	44453.52	.	
Cancer of the brain	1	2.64	44453.52	0.38	(0.01,2.11)
Leukemia	3	3.19	44453.52	0.94	(0.19,2.74)
Lymphomas and multiple myelomas	7	5.9	44453.52	1.19	(0.48,2.45)
Diabetes	3	8.78	44453.52	0.34	(0.07,1)
Cardiovascular disease	96	119.17	44453.52	0.81	(0.65,0.98)
Respiratory disease	20	17.3	44453.52	1.16	(0.71,1.79)
All external	19	13.41	44453.52	1.42	(0.85,2.21)
All cancer	111	105.65	44453.52	1.05	(0.86,1.27)
All causes	286	317.99	44453.52	0.9	(0.8,1.01)
Cancer of the digestive system	18	21.65	44453.52	0.83	(0.49,1.31)

Table B18: SMR analysis results for CSE white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.06	22232.83	.	
Cancer of the stomach	0	0.19	22232.83	.	
Cancer of the colon	1	0.72	22232.83	1.39	(0.04,7.74)
Cancer of the rectum	0	0.1	22232.83	.	
Cancer of the liver	0	0.14	22232.83	.	
Cancer of the pancreas	0	0.36	22232.83	.	
Cancer of the lung	1	2.29	22232.83	0.44	(0.01,2.44)
Cancer of the skin	0	0.35	22232.83	.	
Cancer of the breast	6	3.56	22232.83	1.68	(0.62,3.67)
Cancer of the bladder	0	0.06	22232.83	.	
Cancer of the testis	0	0	22232.83	.	
Cancer of the prostate	0	0	22232.83	.	
Cancer of the kidney	0	0.18	22232.83	.	
Cancer of the brain	0	0.5	22232.83	.	
Leukemia	0	0.5	22232.83	.	
Lymphomas and multiple myelomas	1	0.65	22232.83	1.53	(0.04,8.54)
Diabetes	0	0.85	22232.83	.	
Cardiovascular disease	1	6.59	22232.83	0.15	(0,0.85)
Respiratory disease	0	1.08	22232.83	.	
All external	10	5.89	22232.83	1.7	(0.81,3.12)
All cancer	14	12.62	22232.83	1.11	(0.61,1.86)
All causes	32	33.63	22232.83	0.95	(0.65,1.34)
Cancer of the digestive system	1	1.74	22232.83	0.58	(0.01,3.2)

Table B19: SMR analysis results for TME white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.03	1691.62	.	
Cancer of the stomach	0	0.06	1691.62	.	
Cancer of the colon	0	0.26	1691.62	.	
Cancer of the rectum	0	0.03	1691.62	.	
Cancer of the liver	0	0.04	1691.62	.	
Cancer of the pancreas	0	0.15	1691.62	.	
Cancer of the lung	1	0.76	1691.62	1.32	(0.03,7.37)
Cancer of the skin	0	0.04	1691.62	.	
Cancer of the breast	0	0.67	1691.62	.	
Cancer of the bladder	0	0.03	1691.62	.	
Cancer of the testis	0	0	1691.62	.	
Cancer of the prostate	0	0	1691.62	.	
Cancer of the kidney	0	0.05	1691.62	.	
Cancer of the brain	0	0.09	1691.62	.	
Leukemia	0	0.1	1691.62	.	
Lymphomas and multiple myelomas	0	0.18	1691.62	.	
Diabetes	0	0.26	1691.62	.	
Cardiovascular disease	1	3.29	1691.62	0.3	(0.01,1.7)
Respiratory disease	0	0.53	1691.62	.	
All external	0	0.5	1691.62	.	
All cancer	2	3.21	1691.62	0.62	(0.08,2.25)
All causes	4	9.34	1691.62	0.43	(0.12,1.1)
Cancer of the digestive system	0	0.62	1691.62	.	

Table B20

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Table B21

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Table B22: SMR analysis results for eligible non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.4	16953.31	.	
Cancer of the stomach	1	0.58	16953.31	1.73	(0.04,9.64)
Cancer of the colon	2	1.5	16953.31	1.33	(0.16,4.82)
Cancer of the rectum	0	0.18	16953.31	.	
Cancer of the liver	0	0.33	16953.31	.	
Cancer of the pancreas	0	0.82	16953.31	.	
Cancer of the lung	4	3.37	16953.31	1.19	(0.32,3.04)
Cancer of the skin	0	0.04	16953.31	.	
Cancer of the breast	5	4.7	16953.31	1.06	(0.35,2.48)
Cancer of the bladder	0	0.14	16953.31	.	
Cancer of the testis	0	0	16953.31	.	
Cancer of the prostate	0	0	16953.31	.	
Cancer of the kidney	1	0.25	16953.31	4.07	(0.1,22.68)
Cancer of the brain	1	0.26	16953.31	3.91	(0.1,21.77)
Leukemia	0	0.54	16953.31	.	
Lymphomas and multiple myelomas	0	0.9	16953.31	.	
Diabetes	2	2.89	16953.31	0.69	(0.08,2.5)
Cardiovascular disease	15	23.35	16953.31	0.64	(0.36,1.06)
Respiratory disease	5	1.93	16953.31	2.59	(0.84,6.03)
All external	6	5.86	16953.31	1.02	(0.38,2.23)
All cancer	17	19.14	16953.31	0.89	(0.52,1.42)
All causes	52	71.5	16953.31	0.73	(0.54,0.95)
Cancer of the digestive system	3	4.09	16953.31	0.73	(0.15,2.14)

Table B23: SMR analysis results for exposed non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.06	6159.61	.	
Cancer of the stomach	0	0.12	6159.61	.	
Cancer of the colon	0	0.28	6159.61	.	
Cancer of the rectum	0	0.03	6159.61	.	
Cancer of the liver	0	0.07	6159.61	.	
Cancer of the pancreas	0	0.13	6159.61	.	
Cancer of the lung	1	0.61	6159.61	1.64	(0.04,9.14)
Cancer of the skin	0	0.01	6159.61	.	
Cancer of the breast	1	1.21	6159.61	0.83	(0.02,4.6)
Cancer of the bladder	0	0.02	6159.61	.	
Cancer of the testis	0	0	6159.61	.	
Cancer of the prostate	0	0	6159.61	.	
Cancer of the kidney	1	0.05	6159.61	18.49	(0.47,103.01)
Cancer of the brain	0	0.07	6159.61	.	
Leukemia	0	0.14	6159.61	.	
Lymphomas and multiple myelomas	0	0.2	6159.61	.	
Diabetes	0	0.52	6159.61	.	
Cardiovascular disease	1	4.22	6159.61	0.24	(0.01,1.32)
Respiratory disease	2	0.45	6159.61	4.48	(0.54,16.18)
All external	3	2.25	6159.61	1.33	(0.28,3.9)
All cancer	4	4.07	6159.61	0.98	(0.27,2.51)
All causes	12	16.31	6159.61	0.74	(0.38,1.28)
Cancer of the digestive system	0	0.75	6159.61	.	

Table B24: SMR analysis results for control non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.33	10627.47	.	
Cancer of the stomach	1	0.45	10627.47	2.23	(0.06,12.45)
Cancer of the colon	2	1.19	10627.47	1.68	(0.2,6.05)
Cancer of the rectum	0	0.14	10627.47	.	
Cancer of the liver	0	0.25	10627.47	.	
Cancer of the pancreas	0	0.67	10627.47	.	
Cancer of the lung	3	2.71	10627.47	1.11	(0.23,3.24)
Cancer of the skin	0	0.03	10627.47	.	
Cancer of the breast	4	3.43	10627.47	1.17	(0.32,2.99)
Cancer of the bladder	0	0.11	10627.47	.	
Cancer of the testis	0	0	10627.47	.	
Cancer of the prostate	0	0	10627.47	.	
Cancer of the kidney	0	0.19	10627.47	.	
Cancer of the brain	1	0.19	10627.47	5.38	(0.14,30)
Leukemia	0	0.39	10627.47	.	
Lymphomas and multiple myelomas	0	0.69	10627.47	.	
Diabetes	2	2.32	10627.47	0.86	(0.1,3.11)
Cardiovascular disease	13	18.68	10627.47	0.7	(0.37,1.19)
Respiratory disease	3	1.46	10627.47	2.05	(0.42,5.99)
All external	3	3.56	10627.47	0.84	(0.17,2.46)
All cancer	13	14.77	10627.47	0.88	(0.47,1.51)
All causes	39	54.04	10627.47	0.72	(0.51,0.99)
Cancer of the digestive system	3	3.27	10627.47	0.92	(0.19,2.68)

Table B25: SMR analysis results for CSE non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.04	5349.66	.	
Cancer of the stomach	0	0.09	5349.66	.	
Cancer of the colon	0	0.2	5349.66	.	
Cancer of the rectum	0	0.02	5349.66	.	
Cancer of the liver	0	0.05	5349.66	.	
Cancer of the pancreas	0	0.09	5349.66	.	
Cancer of the lung	1	0.42	5349.66	2.39	(0.06,13.32)
Cancer of the skin	0	0.01	5349.66	.	
Cancer of the breast	1	0.95	5349.66	1.05	(0.03,5.86)
Cancer of the bladder	0	0.01	5349.66	.	
Cancer of the testis	0	0	5349.66	.	
Cancer of the prostate	0	0	5349.66	.	
Cancer of the kidney	1	0.04	5349.66	24.76	(0.63,137.93)
Cancer of the brain	0	0.05	5349.66	.	
Leukemia	0	0.11	5349.66	.	
Lymphomas and multiple myelomas	0	0.15	5349.66	.	
Diabetes	0	0.36	5349.66	.	
Cardiovascular disease	1	3.05	5349.66	0.33	(0.01,1.83)
Respiratory disease	1	0.34	5349.66	2.95	(0.07,16.44)
All external	3	1.97	5349.66	1.52	(0.31,4.45)
All cancer	4	3.04	5349.66	1.32	(0.36,3.37)
All causes	11	12.71	5349.66	0.87	(0.43,1.55)
Cancer of the digestive system	0	0.53	5349.66	.	

Table B26: SMR analysis results for TME non-white females.

Cause	Observed	Expected	Person-Yrs	SMR	95% CI
Cancer of the esophagus	0	0.02	809.96	.	
Cancer of the stomach	0	0.03	809.96	.	
Cancer of the colon	0	0.08	809.96	.	
Cancer of the rectum	0	0.01	809.96	.	
Cancer of the liver	0	0.02	809.96	.	
Cancer of the pancreas	0	0.04	809.96	.	
Cancer of the lung	0	0.19	809.96	.	
Cancer of the skin	0	0	809.96	.	
Cancer of the breast	0	0.26	809.96	.	
Cancer of the bladder	0	0.01	809.96	.	
Cancer of the testis	0	0	809.96	.	
Cancer of the prostate	0	0	809.96	.	
Cancer of the kidney	0	0.01	809.96	.	
Cancer of the brain	0	0.01	809.96	.	
Leukemia	0	0.03	809.96	.	
Lymphomas and multiple myelomas	0	0.05	809.96	.	
Diabetes	0	0.16	809.96	.	
Cardiovascular disease	0	1.17	809.96	.	
Respiratory disease	1	0.11	809.96	9.3	(0.24,51.84)
All external	0	0.28	809.96	.	
All cancer	0	1.03	809.96	.	
All causes	1	3.6	809.96	0.28	(0.01,1.55)
Cancer of the digestive system	0	0.22	809.96	.	

Table B27

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Table B28

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Appendix C, Table 1. Changes in SMRs in the Control Group

		Differences		Old Figures			New Figures		
Race/ Gender	Cause	Observed	SMR	Observed	SMR	95% CL	Observed	SMR	95% CL
NWM	Ca esophogus	-1	-0.42	2	0.83	(0.1,2.99)	1	0.41	(0.01,2.3)
NWM	Ca lung	-1	-0.07	10	0.67	(0.32,1.23)	9	0.6	(0.28,1.14)
NWM	Leukemia	-1		1	0.87	(0.02,4.87)	0	.	
NWM	Cardiovascular disease	-3	-0.04	56	0.85	(0.64,1.11)	53	0.81	(0.6,1.06)
NWM	All external	-1	-0.04	25	0.9	(0.58,1.33)	24	0.86	(0.55,1.29)
NWM	All cancer	-3	-0.07	29	0.69	(0.46,0.99)	26	0.62	(0.4,0.9)
NWM	All causes	-9	-0.05	144	0.72	(0.61,0.85)	135	0.67	(0.56,0.8)
NWM	Ca digestive	-1	-0.08	9	0.77	(0.35,1.47)	8	0.69	(0.3,1.36)
WF	Ca lung	-2	-0.08	41	1.71	(1.23,2.32)	39	1.63	(1.16,2.22)
WF	Lymphomas and multiple mylelomas	-1	-0.17	8	1.36	(0.59,2.67)	7	1.19	(0.48,2.45)
WF	Cardiovascular disease	-1	0	97	0.81	(0.66,0.99)	96	0.81	(0.65,0.98)
WF	All cancer	-4	-0.04	115	1.09	(0.9,1.31)	111	1.05	(0.86,1.27)
WF	All causes	-6	-0.02	292	0.92	(0.82,1.03)	286	0.9	(0.8,1.01)
WM	Ca colon	-1	-0.03	39	1.11	(0.79,1.52)	38	1.08	(0.77,1.49)
WM	Ca pancreas	-2	-0.09	26	1.28	(0.84,1.88)	24	1.19	(0.76,1.76)
WM	Ca lung	-5	-0.03	151	1	(0.85,1.18)	146	0.97	(0.82,1.14)
WM	Ca testis	-1	-0.73	3	2.21	(0.46,6.47)	2	1.48	(0.18,5.33)
WM	Ca prostate	-1	-0.04	29	1.01	(0.67,1.44)	28	0.97	(0.65,1.4)
WM	Ca kidney	-1	-0.09	12	1.07	(0.55,1.86)	11	0.98	(0.49,1.75)
WM	Lymphomas and multiple mylelomas	-2	-0.07	27	1.03	(0.68,1.51)	25	0.96	(0.62,1.41)
WM	Diabetes	-1	-0.03	21	0.7	(0.44,1.08)	20	0.67	(0.41,1.04)
WM	Cardiovascular disease	-25	-0.03	583	0.87	(0.8,0.95)	558	0.84	(0.77,0.91)
WM	Respiratory disease	-2	-0.03	69	0.9	(0.7,1.14)	67	0.87	(0.68,1.11)
WM	All external	-10	-0.06	157	0.93	(0.79,1.09)	147	0.87	(0.74,1.03)
WM	All cancer	-15	-0.04	452	1.09	(0.99,1.19)	437	1.05	(0.95,1.15)
WM	All causes	-57	-0.03	1495	0.91	(0.87,0.96)	1438	0.88	(0.83,0.93)
WM	Ca digestive	-4	-0.04	127	1.28	(1.07,1.53)	123	1.24	(1.03,1.48)

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